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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 19 1955

EXCHANGE TRANSFUSION IN HAEMOLYTIC DISEASE OF THE NEWBORN

BY

WILLIAM WALKER, M.D. AND G. A. NELIGAN, B.M., M.R.C.P.

(From the Department of Child Health, University of Durham)

PART I. TREATMENT

In the treatment of haemolytic disease of the newborn we regard it as proved that early exchange transfusion is superior to simple transfusion. The evidence in support of this was obtained in controlled trials carried out in various British centres between October, 1949, and August, 1951 (Mollison and Walker, 1952).

The Newcastle-upon-Tyne cases that formed part of these trials provide a comparison between early exchange and late simple transfusion. All infants in this centre were the result of spontaneous delivery. Those with a cord Hb level of 14.8 g.% or less were selected at random for either exchange or simple transfusion. When indicated, exchange transfusion of at least 60 ml. per lb. (132 ml. per kg.) body weight was carried out within nine hours of birth. A total of 86 children were included in the trial (Table I). In the group selected for simple transfusion this was given if the Hb level fell to 11 g.% during the first fourteen days of life. Apart from the type of transfusion given, all babies received identical care.

TABLE I.—*A Controlled Trial of Exchange and Simple Transfusion in 86 Infants with Haemolytic Disease (National Investigation, Newcastle-upon-Tyne Centre, 1949–52)*

	No. of Cases	No. with Kernicterus	No. of Deaths
Simple transfusion ..	42	9	13
Exchange „ ..	44	0	2

Of the 42 babies treated by simple transfusion, 13 died, whereas of the 44 treated by exchange transfusion only two died. Nine of the 42 treated by simple transfusion developed kernicterus, whereas no baby in the exchange transfusion group did so. The probability of such differences being due to chance is about 1 in 1,000.

Five infants had birth weights of 5½ lb. (2.5 kg.) or less. By chance, all were treated by simple transfusion and four died with kernicterus. We have calculated the probabilities after excluding these cases. The findings are still significantly in favour of exchange transfusion, but of course to a less degree. In relation to both mortality and kernicterus P now equals 0.02–0.01.

The purpose of this communication is to describe our experience of 250 consecutive cases treated by adequate exchange transfusion between March, 1947, and March, 1954. The evaluation of the procedure depends on various factors, while its effectiveness is closely related to details of technique. Our experience will therefore be presented in two parts—the first dealing with indications and results, and the second with technique. We are concerned essentially with the application of our collected observations to daily practice.

Principles

From the start we felt that exchange transfusion was indicated and justified only in the more severely affected cases of haemolytic disease of the newborn, and throughout have tried to confine it to infants in whom there was a real risk of death or in whom transfusion was almost certain to be required sooner or later.

It has been our practice to use partly packed "bank" blood from either sex, and all but one of our 250 adequate exchange transfusions have been performed by the umbilical route, as will be described in Part II.

We have aimed to carry out, within the first nine hours of life, an exchange of 80 ml. per lb. (176 ml. per kg.) body weight. This amount was decided upon because it is equivalent to at least two blood volumes, and Wiener and Wexler (1946) had calculated that this gave 85% exchange, while the use of 120 ml. per lb. (264 ml. per kg.) raises the degree of exchange only by a further 8%. The period of nine hours was chosen because it was one of the rules governing the national trials, and we found that it was a convenient time limit and gave good results. Sometimes, for one reason or another, it is not possible to complete the full 80 ml. per lb. (176 ml. per kg.) and we have accepted as "adequate" any transfusion resulting in the exchange of 60 ml. per lb. (132 ml. per kg.), as again this was one of the rules governing the national trials. Anything less than 60 ml. per lb. (132 ml. per kg.) has been classed as "inadequate." Obviously the nine-hour time limit can only apply to infants seen at or shortly after birth, but we have performed exchange transfusion on many infants seen later than this, and in such cases have begun treatment as early as possible. The effectiveness of exchange transfusion must depend to some extent on the volume of blood exchanged and the age at which it is carried out. We have not made a special point of trying to assess these factors, and any observations that we have made concerning them are incidental.

Material

The material on which this report is based is derived from 272 cases* selected for exchange transfusion between March, 1947, and March, 1954. In 1947 and 1948 only eight adequate exchanges were performed, while 19 were inadequate. During the next five years there have been 242 adequate transfusions and only three inadequate—two in 1949 and

*Cases from the Princess Mary Maternity Hospital, General Hospital, and Babies' Hospital, Newcastle-upon-Tyne, and the Queen Elizabeth Hospital, Gateshead, and a small number treated by us in other hospitals outside this area.

one in 1951. This is a reflection of the increasing experience with the technique and improvement in preparation and maintenance of equipment.

Premature induction has never formed part of our routine practice, but recently we have performed induction in cases in which there was a history of a previous stillbirth due to haemolytic disease and in which the father was homozygous Rh positive. Our experience of this type of case is limited to 10, so it is obviously much too early to draw conclusions from the results. Four of the resulting infants were treated by exchange transfusion and are included in this series. Any other premature infants in this series were the result of spontaneous premature labour or a pregnancy terminated prematurely for some independent obstetrical indication.

Indications For Exchange Transfusion

We have relied on certain criteria of severity to decide if treatment was required in a particular case, and in the light of experience have found it necessary to change these criteria on two occasions.

Our indications for exchange transfusion have been as follows, and they apply both for mature and for premature infants.

1. March, 1947, to September, 1949

(*a*) Any first affected infant showing jaundice or other clinical signs of disease within eight hours of birth. (*b*) Any subsequent affected infants showing clinical evidence of disease within the first twenty-four hours. These criteria were helpful, but depended on signs which could be difficult to assess and missed some cases that developed kernicterus, while perhaps 20% were treated unnecessarily.

2. October, 1949, to August, 1951

This was the period of the national trials, and the criterion used was a cord Hb value of 14.8 g.% or less. Eighty-six cases fulfilled this condition, but only 44 received exchange transfusion; the remaining 42 selected at random served as controls and received simple transfusion only for the treatment of severe anaemia.

The level of 14.8 g.% proved satisfactory in that only 4 of the 42 control cases did not require treatment. All four had levels between 13.2 and 14.8 g.%. As the other 11 cases in this range required treatment, we felt justified in retaining the criterion of 14.8 g.%, considering it advisable to allow for error in Hb determination, even if erring on the side of overtreatment. Moreover, 14.8 g.% corresponds with the lower limit of cord Hb in the majority of normal infants.

Ninety-five other infants with cord Hb values greater than 14.8 g.% were born during this period. None received early treatment. Twenty-three had cord Hb levels higher than 17.7 g.%. None died; indeed, only one required transfusion. We therefore felt it safe to leave untreated any infant with a cord Hb level greater than 17.7 g.%.

We were disturbed, however, to find that of 72 infants with cord Hb values between 14.8 and 17.7 g.%, five developed kernicterus, while 16 others eventually required transfusion for the relief of anaemia. One infant with a cord Hb level of 17.5 g.% died with kernicterus, while the Hb values in infants requiring transfusion were evenly distributed throughout this range—that is, 5 out of 20 with cord Hb values between 14.8 and 15.5 g.% and 16 out of 52 with values between 15.5 and 17.7 g.% required treatment. We therefore felt that the criterion of cord Hb alone was not satisfactory, because if the level was set high enough to include all infants at risk it would mean subjecting a large number to unnecessary treatment.

Between the levels of 14.8 and 17.7 g.% some different means of selecting cases for treatment was therefore required. It was in this respect that the cord bilirubin level promised to be of value. We had made cord bilirubin estimations on 52 infants in this range. The lowest level associated with the development of kernicterus was 2.8 mg. per 100 ml. In fact, 13 infants had cord bilirubin levels of 2.8 mg. per 100 ml. or more, and three of these developed kernicterus, while five others required transfusions. In contrast, only 4 out of 40 infants with cord bilirubin levels of less than 2.8 mg. per 100 ml. required treatment. There were no deaths in this group and none required treatment in the first two weeks of life.

We therefore decided to adopt new criteria for exchange transfusion, and, as relatively few cases would be involved, considered that a controlled trial was not advisable: rather, we would judge their value by dealing with the prevention of kernicterus and the proportion of cases surviving without treatment.

3. September, 1951, to March, 1954

The criteria, still based on cord blood examination, were extended to include any infant with a cord Hb level of 14.8 g.% or less and any infants with cord Hb level between 14.8 and 17.7 g.% associated with a cord bilirubin level of 2.8 mg. per 100 ml. or more.

Since adopting these criteria, we have not seen a single case of kernicterus in a baby with less severe disease than they define. We cannot, of course, say accurately how many babies have been treated unnecessarily, but there has certainly been no mortality among the babies treated because of a high bilirubin level.

In this period we obtained cord blood samples suitable for both Hb and bilirubin estimation from 264 live-born infants with haemolytic disease of the newborn: 162 (61%) met the above criteria for exchange transfusion. A further seven infants were eventually transfused because of anaemia. No infant left without exchange transfusion died, and none required transfusion within the first three weeks of life. Altogether, 95 (36%) survived without any treatment at all. This corresponds closely with the expected proportion not requiring treatment. In a local series (Walker, 1950) collected between 1947 and 1949, when exchange transfusion was being used in only a minority of cases, 42% survived without treatment, while during the period of the national trials 43% survived without treatment.

Present Indications For Exchange Transfusion When Full Cord Blood Results Are Not Available

In cases in which for any reason the cord Hb or bilirubin level alone was available, this has been used as a guide in assessing the severity of disease. Nine infants with bilirubin levels higher than 2.7 mg. per 100 ml., but whose cord Hb was not known, were born at home and seen too late to be treated by exchange transfusion. Two died with kernicterus, three required simple transfusion, while the other four survived without treatment.

When neither cord Hb nor bilirubin estimations were available we have regarded the onset of clinical disease in the first eight hours of life as an indication for exchange transfusion, provided that evidence of brain damage was not already manifest when the infant was first seen.

In infants in whom neither the cord blood results nor the accurate information regarding the early clinical picture were available, Hb and bilirubin estimations on venous blood assisted in assessing the severity of the disease.

Indications For Repeated Exchange Transfusion

Unfortunately, early adequate exchange transfusion does not guarantee that kernicterus will be prevented. The known association of kernicterus and deep jaundice has consequently led to repeated exchange transfusions being recommended "in infants with severe and rapidly increasing jaundice, or if the bilirubin is more than 20 mg. per 100 ml. or likely to go that high." Using these criteria, Diamond *et al.* (1952) found it necessary to do multiple exchange transfusions in 20% of their cases.

In our experience kernicterus has occurred in only 2 out of 196 mature infants but in 3 out of 22 premature infants

treated by early adequate exchange transfusion. This disproportionate risk between mature and premature infants corresponds with our observation that after exchange transfusion 45% of premature infants developed deep jaundice; whereas only 13% of mature infants did so. We therefore feel that repeated exchange transfusion should be necessary only in a very small proportion of cases, and these mainly premature infants. The bilirubin level during the first week of life will probably prove the most satisfactory criterion for selecting cases for repeated exchange transfusion, and we have provisionally taken 25 mg. per 100 ml. as our indication.

Up to March, 1954, we had performed repeated exchange transfusion in only four infants. Three were born at labour induced surgically because of a previous history of stillbirth due to haemolytic disease of the newborn and because the father was homozygous Rh positive.

The fourth, a mature infant, was transfused with blood that, in retrospect, we thought had been overheated. The baby became deeply jaundiced and developed haemoglobinuria the day following exchange transfusion. As intense intravascular haemolysis was occurring, we decided to perform a second exchange transfusion. The response was dramatic; the bilirubin fell from 32.5 to 12.6 mg. per 100 ml. during the procedure. Haemoglobinaemia disappeared immediately and no subsequent haemoglobinuria occurred. Eighteen hours after the second exchange transfusion the bilirubin was 16 mg. per 100 ml., but fell thereafter, and jaundice had practically disappeared three days after the second transfusion.

Altogether in 1954 eight premature infants were treated by exchange transfusion, and two of these required a further exchange transfusion, whereas only 5 of 79 mature infants treated by exchange transfusion required further exchange. It should be pointed out, however, that two of these five were the result of premature induction at 35 weeks' gestation, while a third was first treated at the age of 4 days when the bilirubin level was 60 mg. per 100 ml.

Age at Time of Exchange Transfusion

It has always been our aim to start exchange transfusion within the first nine hours of life, but in 28 cases transfusion was not started until later, usually because the baby was born at home with resultant unavoidable delay. One such case, a mature baby, received an exchange transfusion of 80 ml. per lb. (176 ml. per kg.) at the age of 19 hours, but subsequently died from pulmonary haemorrhage and kernicterus. Of the 222 treated within nine hours of birth, 196 were mature* infants, and only two of these developed kernicterus.

Wallerstein (1947) recorded four deaths due to kernicterus among 27 cases treated by exchange transfusion. All four were treated later than twenty-four hours, when jaundice was already well marked.

We regard it as convenient and satisfactory to start exchange transfusion within the first nine hours of life in infants born in hospital and diagnosed by means of tests on cord blood. We have formed the strong impression that the general condition of infants with haemolytic disease improves during the first few hours of life—as might be expected from experience of the normal baby. If delivery has been difficult, or if the infant's condition is poor for reasons other than haemolytic disease, this preliminary period of acclimatization is all the more important, and oxygen therapy may be helpful. After nine hours we have observed a tendency for the general condition to deteriorate, and in particular a number of babies in good condition at birth were very ill by the time they were admitted to hospital for treatment.

On the other hand, immediate treatment may be called for, as in six cases in which we started the transfusion within the first hour of life. Each infant was desperately ill at birth, with a Hb level less than 6 g.% and signs of heart failure. None had shown any improvement in the short interval before treatment started. Three survived, and the clinical improvement during the transfusion was most dramatic. The other three died during the transfusion, and two of these were found at necropsy to be hydropic.

Within these limits we feel that the actual time for exchange transfusion can be decided by convenience and by clinical observation of the individual baby, and prefer, as a rule, to begin treatment at about four to six hours.

*Weighing more than 5½ lb. (2.5 kg.) at birth.

Volume of Blood Exchanged

As stated previously, we have always aimed to exchange 80 ml. per lb. (176 ml. per kg.) body weight, or twice the baby's estimated blood volume. This accords with the recommendations of various workers (Wiener and Wexler, 1946; Wallerstein, 1947; Diamond *et al.*, 1952), and should result in about 85% of the baby's blood being replaced by donor blood. The blood required, except in babies weighing more than 8½ lb. (3.9 kg.), can be obtained from two bottles of partly packed "bank" blood. We have not varied the volume of blood exchanged in relation to the cell volume of infant and donor blood, as suggested by Veall and Mollison (1950); therefore, there has been a relatively greater degree of replacement in the more anaemic cases, and this seems to us to be an advantage. The application of Veall and Mollison's nomogram will, however, enable adequate exchange transfusion to be carried out with minimal quantities of blood. Wiener and Wexler (1949) suggested that in very severely affected infants as much as 1,000 ml. should be exchanged, but it seems to us that the slight increase in the completeness of exchange so achieved is offset by the risks of the longer procedure. Indeed, the same authors (1951) later suggested that an exchange of 100–150 ml. of packed red cells was adequate. It is well to remember that as the exchange transfusion progresses, so the relative effectiveness of each 10 ml. of blood exchanged diminishes. Therefore, if the infant's condition gives cause for anxiety towards the end of transfusion it may be wiser to stop, rather than to carry on in an effort to reach the target figure.

Our secondary aim in performing exchange transfusion has been to achieve a final Hb level of between 15 and 17 g.%. This reduces the possibility of further transfusion being required, but, more important, it depresses erythropoiesis and the production of cells liable to rapid haemolysis.

We have made no systematic observations on the relationship between percentage exchange and mortality, but in the period 1947–9, 20 cases selected because of early clinical disease received inadequate exchange transfusions. Seven of the 20 receiving inadequate exchange transfusions died, while 18 of the 51 treated by simple transfusion died—that is, a mortality rate of 35% in each group. Three cases of kernicterus occurred in the exchange and 11 in the simple transfusion groups. It seems, therefore, that exchange transfusion of less than 60 ml. per lb. (132 ml. per kg.) gives no better result than simple transfusion.

Davies *et al.* (1953) claimed that, in their experience, an exchange of 60 ml. per lb. (132 ml. per kg.) did not prevent kernicterus; whereas 80–100 ml. per lb. (176–220 ml. per kg.) exchange or two exchanges each of 60 ml. per lb. (132 ml. per kg.) did so.

Mortality in Cases Treated by Exchange Transfusion

Even accepting that adequate exchange transfusion is superior to simple transfusion, we still require to assess the part it may be expected to play in the management of haemolytic disease. Can exchange transfusion be recommended as a safe routine procedure? Are there special risks associated with the method itself? Are there some cases in which exchange transfusion is ineffective? If adopted as the treatment of choice for all cases likely to require treatment, what order of improvement in survival can be expected?

Although the results of many series of cases treated by exchange transfusion have been published (Hart, 1925;

Wallerstein, 1946, 1947, 1948; Wiener and Wexler, 1946, 1949; Diamond, 1947, 1948; Mollison and Cutbush, 1948; Diamond *et al.*, 1952), the answers to these questions are not readily found. The reason is that many of the series are small and highly selected, so that they do not represent the disease as a whole, nor is one series necessarily comparable with another.

Certain earlier reports cannot be accepted at their face value, because standards of diagnosis were changing as well as methods of treatment. The pitfalls of these interpretations are illustrated by Diamond (1947), who reported reduction in mortality with changes in treatment, as follows:

Period	Treatment	Mortality
Pre-1941	Simple transfusion (probably Rh positive)	40%
1942–4	,, ,, (Rh negative)	30%
1944–6	Premature induction and simple transfusion (Rh negative)	20%
1947–	Premature induction and exchange transfusion (severe cases excluded)	10%

It seems possible that the reduction in overall mortality was not due solely to improvement in treatment, but could, in part, be explained by improvement in diagnosis. Before 1941, when the diagnosis was made on clinical grounds, only severe cases, mainly those presenting the clinical picture of icterus gravis, would be included. With the increasing use of serological methods of diagnosis one would expect an increasing proportion of the recognized cases to be mildly affected, with a corresponding reduction in mortality irrespective of improvements in treatment. In confirmation of this hypothesis, we found, during a survey of cases in the Northern Region for 1947–9 (Walker, 1950) that there was a mortality rate of 40% in cases diagnosed clinically as icterus gravis, but of only 15% in the group as a whole, which included cases diagnosed on serological evidence alone.

The published series vary in size from 9 to 208 cases and the mortality rate from 6 to 32%. Many are too small to allow evaluation of the results, while in most the indications for exchange transfusion are so numerous and varied that they allow considerable freedom of interpretation and consequent intrusion of personal bias.

More recently, other factors—for example, the use of female blood and the performance of multiple exchange transfusion—have been reported as bringing about a fall in mortality.

Results

The following are our results in all cases in which exchange transfusion of at least 60 ml. per lb. (132 ml. per kg.) was carried out.

In the past five years only 3 out of 245 infants selected for exchange transfusion have not received a transfusion of at least 60 ml. per lb. (132 ml. per kg.). Two were technical failures, while the third, born *in extremis*, died before the transfusion could be completed. It is known that premature infants are at greater risk than mature babies, and we think that infants born in hospitals offering special facilities stand a better chance than infants admitted from "outside"; we therefore present our results in three groups. No case has been omitted, and none has been included in more than one group.

Group I.—Premature Infants. All infants with birth weights of 5½ lb. (2.5 kg.) or less are included. As there are so few cases in this group, we have not subdivided them in relation to the means by which they were selected for exchange transfusion, nor by the age at which this was carried out.

Group II.—Mature infants born at home, or in hospitals not affording special facilities. These cases were selected for treatment usually because of the early appearance of clinical disease as already defined, or, in some more recent cases, because the cord blood specimen taken routinely from the infants of *all* Rh-negative mothers was found to be Coombs-positive and to have a bilirubin level of 2.8 mg. per 100 ml. or more. Many were not treated until after the age of nine hours.

Group III.—Mature infants born in hospitals affording special facilities, selected on the basis of cord Hb and bilirubin levels and treated within nine hours of birth. This group includes all the national trial cases.

In Table II we have classified deaths as due to haemolytic disease or to other causes. It is realized that when death occurs in a baby suffering from haemolytic disease of the newborn one can never be absolutely certain that this disease played no part in causing death. Post-mortem examinations were made in all fatal cases, and the cause of death recorded is that given by the pathologist.

The causes of death are shown in Tables III and IV, and brief clinical notes on these cases are included in an Appendix.

None of these infants had evidence of kernicterus at necropsy. All but the first and last cases were very ill at the time of transfusion, and in them the diagnosis eventually recorded as the cause of death was made before treatment was started.

TABLE II.—*Results in 250 Cases of Haemolytic Disease of the Newborn Treated by Adequate Exchange Transfusion*

Group	No. of Cases	Neonatal Deaths		Mortality Due H.D.N.	Kernicterus
		Due to H.D.N.	Other Causes		
I ..	22*	6	2	27%	2 died (A and WK) 1 survived (Mu)
II ..	37	4	3	11%	1 died (G)
III ..	191	5	3	2·6%	1 survived (F)
Total	250	15	8	6%	5

* 3 multiple exchange transfusions.

TABLE III.—*Deaths Not Attributed to Haemolytic Disease of the Newborn*

Group I ..	Cerebral haemorrhage	H
	,, birth injury	McA
,, II ..	Pneumonia	Th
	Cerebral birth injury	T
	Subdural haematoma	A
,, III ..	Atelectasis	K
	Vernix inhalation	P
	Overlaid	F

TABLE IV.—*Deaths* (15) *Attributed to Haemolytic Disease of the Newborn*

Group	Hydrops Foetalis	Kern-icterus	Heart Failure	General-ized Bleeding	Cardiac Arrest	Cir-rhosis of Liver	Not Known
I ..	2 (WI) (E)	2 (WK) (A)	1 (O'H)	—	1 (Be)	—	—
II ..	—	1 (G)	3 (DO) (D) (ATH)	—	—	—	—
III ..	—	—	1 (B)	2 (H) (Da)	—	1 (O)*	1 (L)
Total	2	3	5	2	1	1	1

* Died at 6 months with terminal respiratory infection. At necropsy, cytomegalic inclusion bodies were found. In the absence of proof to the contrary, this death has been attributed to haemolytic disease. No abnormality of the central nervous system could be demonstrated histologically.

Severity of Disease

The severity of disease in any particular series may differ from that in another, and this will obviously influence the results. The distribution of the factors most likely to influence the results—birth weight (Fig. 1), cord Hb (Fig. 2), and sex of baby—are shown, to serve as a means of comparison with other series.

Follow-up

First Six Weeks.—All infants were kept under observation during the first six weeks, and during this period 28 out of 229 (12%) required "topping-up" transfusion because the capillary haemoglobin level fell to less than 8.5 g.%. In 10 of these the explanation was that the infants were very severely affected and therefore exchange transfusion was

completed at a negative balance. In the remainder we could find no particular reason for the development of anaemia, but none required secondary transfusion during the first three weeks of life. These findings are in contrast to those of Davies *et al.* (1953), who found "topping-up" transfusion necessary in 60% of cases.

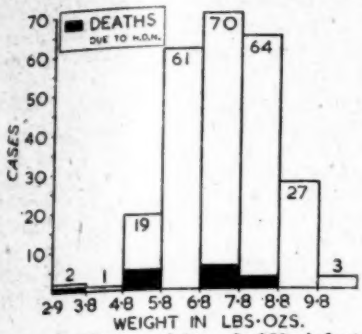

FIG. 1.—Birth weight of 250 infants treated by exchange transfusion. Males, 128; female, 116. Weight was not recorded in three cases.

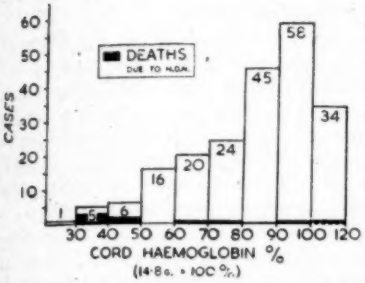

FIG. 2.—Severity of H.D.N. measured by cord Hb in 209 infants treated by exchange transfusion.

Ten to Fourteen Months.—We have tried to see the first 200 cases at the age of about 1 year, in order to assess development by means of simple observations and questioning. All survivors attended for follow-up, except 10 who lived at a distance. The mothers of all 10 wrote telling us of the child's development. In any cases in which there was any question of abnormality the infant was seen by an independent paediatrician. Two infants were regarded as definite cases of kernicterus, one a mature baby and one a premature infant (F and Mu) and a third was regarded as a probable case (McD.). Another infant was mentally defective, but was regarded as a primary ament, not due to haemolytic disease. The remainder were judged to be normal children.

(Since this paper was submitted the remaining 50 cases have been seen at the age of 6 months or more, and all are apparently normal.)

Later Follow-up.—Some of these infants form part of a group being followed up for a longer period, and the results will be published later.

Conclusions

Although various methods of treating haemolytic disease of the newborn have been suggested from time to time (Hardwick and Lloyd, 1941; Homburger, 1946; Kariher and Miller, 1947; Carter, 1949, 1951; Pickles, 1949), so far there is no means of preventing immunization in an Rh-negative woman, or of protecting an Rh-positive foetus against the action of antibodies, once formed. Exchange transfusion, first recommended by Hart (1925), has, however, proved of great value in treating affected infants.

Exchange transfusion is a safe routine procedure and is recommended as the treatment of choice for the 60% of liveborn affected infants requiring treatment.

In experienced hands exchange transfusion carries a very low operative risk, and this risk is practically confined to infants whose chance of survival would be very poor if treated by other means.

In our experience, premature infants have a significantly worse chance of survival than mature infants, owing mainly to the increased risk of kernicterus. Therefore, prematurity should be avoided whenever possible.

In areas where exchange transfusion is adopted as the treatment of choice for all cases likely to require treatment, a survival rate of 98% of all live-born affected infants can be expected. Confirmation of this claim is to be found from consideration of the two years 1952 and 1953 (Walker and Murray, 1954), during which 217 infants with haemolytic disease were born in the Newcastle hospitals: 15 were premature, 125 (58%) were treated by exchange transfusion, while five more (2%) required simple transfusion. Seven died, but only four of these deaths were regarded as due to haemolytic disease—a mortality rate of 2%.

We believe that cord Hb and bilirubin levels permit selection of practically all cases likely to require treatment, and consider that exchange transfusion of 80 ml. per lb. (176 ml. per kg.) body weight, carried out within nine hours of birth, is indicated in these cases.

APPENDIX: CASE SUMMARIES FOR FATAL CASES

Not Attributed to Haemolytic Disease of the Newborn

Group I

H.—B. wt. 5 lb. (2.3 kg.). Cord Hb 12.7 g.%. Cord bilirubin 3 mg. per 100 ml. Infant became ill on the fourth day and died. Mild jaundice (bilirubin 3.6 mg. per 100 ml.) at time of death. P.M.: Cerebral haemorrhage; no kernicterus.

McA.—B. wt. 3 lb. (1.4 kg.). Cord bilirubin 5.6 mg. per 100 ml. Normal respiration never established; cyanosed whenever removed from oxygen; died during exchange transfusion. P.M.: Cerebral birth injury, medullary herniation.

Group II

Th.—B. wt. 6 lb. 8 oz. (2.9 kg.). A sick child with moaning respiration, treated at 11 hours. Died at 18 hours. P.M.: Bilateral bronchopneumonia; sticky mucus in trachea; haemorrhagic exudate in pleural cavities.

T.—B. wt. 6 lb. 12 oz. (3.1 kg.). Difficult delivery with foetal distress. Died at 2 days. P.M.: Cerebral birth injury.

A.—B. wt. 8 lb. 12 oz. (4 kg.). Precipitate labour. Severe haemolytic disease and respiratory difficulty regarded as cerebral in origin. Died at 2 days. P.M.: Cerebral birth injury; large subdural haematoma.

Group III

K.—B. wt. 6 lb. 1 oz. (2.7 kg.). Cord Hb 8 g.%. Cord bilirubin 15 mg. per 100 ml. Died at 3 days. P.M.: Atelectasis; pneumonia; no evidence of kernicterus, heart failure, or haemorrhage.

P.—B. wt. 7 lb. (3.2 kg.). Cord Hb 8 g.%. Admitted with marked cyanosis and asphyxial haemorrhages. P.M.: Atelectasis.

F.—B. wt. 6 lb. 9 oz. (3 kg.). Cord Hb 16 g.%. Cord bilirubin 4.1 mg. per 100 ml. Overlaid one week after discharge aged 3 weeks.

Attributed to Haemolytic Disease of the Newborn

Group I

WI.—B. wt. 3 lb. 3 oz. (1.4 kg.). Cord Hb 4.6 g.%. Cord bilirubin 2.7 mg. per 100 ml. Twin of classical hydrops foetalis. Died during exchange transfusion. P.M.: Hydrops foetalis.

E.—B. wt. 4 lb. 10 oz. (2.1 kg.). Hb 4.8 g.%. Cord bilirubin 6.5 mg. per 100 ml. Died at end of exchange transfusion. P.M.: Hydrops foetalis.

WK.—B. wt. 5 lb. 8 oz. (2.5 kg.). Cord bilirubin 4.1 mg. per 100 ml. Died at 4 days, when bilirubin was 30 mg. per 100 ml. P.M.: Kernicterus.

A.—B. wt. 5 lb. (2.3 kg.). Cord Hb 17 g.%. Cord bilirubin 7.4 mg. per 100 ml. Died, deeply jaundiced, at 63 hours. P.M.: Kernicterus.

O'H.—B. wt. 5 lb. 3 oz. (2.4 kg.). A very ill infant that died at end of exchange transfusion. P.M.: Heart failure.

Be.—B. wt. 5 lb. (2.3 kg.). Cord Hb 11 g.%. Cord bilirubin 4.8 mg. per 100 ml. An infant the result of premature induction at 35 weeks, because of previous history of stillbirth due to haemolytic disease of the newborn. Second exchange transfusion was performed at 47 hours and the infant died suddenly during the procedure. We regard this death as caused by cardiac arrest due to hyperpotassaemia. P.M.: Nothing abnormal detected. This case is described more fully in Part II.

Group II

G.—B. wt. 7 lb. 3 oz. (3.3 kg.). Exchange transfusion at 19 hours, when deeply jaundiced. Died at 48 hours with kernicterus and massive pulmonary haemorrhage.

Do.—B. wt. 7 lb. 6 oz. (3.3 kg.). Given additional 70 ml. of blood at end of exchange transfusion. P.M.: Heart failure and dilated right heart.

D.—B. wt. 7 lb. 1 oz. (3.2 kg.). A very ill baby treated immediately after delivery. Collapsed and died during transfusion. P.M.: ? Heart failure.

Ath.—B. wt. 7 lb. 2 oz. (3.2 kg.). Very ill on admission, suddenly collapsed and died during exchange transfusion. P.M.: Heart failure.

Group III

B.—B. wt. 8 lb. (3.6 kg.). Cord Hb 5.9 g.%. Cord bilirubin 11.5 mg. per 100 ml. A very ill baby that improved dramatically during exchange transfusion but suddenly, when the transfusion was almost completed, collapsed and died. P.M.: ? Heart failure.

H.—B. wt. 7 lb. 8 oz. (3.4 kg.). Cord Hb 10.3 g.%. Cord bilirubin 1.9 mg. per 100 ml. Deteriorated towards end of exchange transfusion. Was semicomatose, with moaning respiration for 12 hours; death occurred. Had been given prophylactic vitamin K. P.M.: Haemorrhage into abdomen, pleura, pericardium, cranium; umbilical vein intact; hepatic necrosis.

Da.—B. wt. 7 lb. 4 oz. (3.3 kg.). Cord Hb 5.7 g.%. Cord bilirubin 4.9 mg. per 100 ml. Given prophylactic vitamin K. Twenty-four hours after exchange transfusion had fit, and six hours later developed pulmonary haemorrhage and died. P.M.: Haemorrhage into lungs, adrenal, kidney, and stomach; liver necrosis.

O.—Cord Hb 4.5 g.%. Bilirubin 8 mg. per 100 ml. Progressive jaundice and hepatosplenomegaly. Died aged 6 months. P.M.: Cytomegalic inclusion disease.

L.—B. wt. 8 lb. 2 oz. (3.7 kg.). Cord Hb 14 g.%. Cord bilirubin 2.9 mg. per 100 ml. Sudden death fifty minutes after exchange transfusion. P.M.: Nothing abnormal detected.

PART II. TECHNIQUE

The results of exchange transfusion in cases of haemolytic disease of the newborn, presented as Part I of this article, have convinced us that early adequate exchange transfusion is the treatment of choice for all cases in which treatment is likely to be required. The primary justification of this conviction lies in the infant's greater chance of survival, but exchange transfusion also has the very real advantage that it will avoid the necessity for frequent haemoglobin estimations and perhaps multiple transfusions.

The successful application of the principles set out in Part I depends on the performance of a series of technical procedures. In the past seven years we have attempted exchange transfusion in 272 babies, and 250 of these have been technically satisfactory. Only 3 of the 22 failures have occurred in the last five years, and this we attribute to increased experience of the procedure and improved maintenance of apparatus.

We have tried to develop a simple straightforward technique and hope that a description of the method we use and the difficulties we have encountered may be of help to others concerned with the practical management of these cases.

General Routine Governing Treatment

1. The disease is predicted antenatally by serological tests, and delivery in a hospital providing special facilities for the care of these infants is advised.

2. The umbilical cord is clamped about 15 cm. from the abdominal wall as soon as possible after delivery. Using a dry syringe and No. 1 needle, the midwife or the doctor collects 10 ml. of blood from the umbilical vein on the maternal side of the clamp. Half of the blood is transferred to a plain tube for serological tests, and half into one containing dry anticoagulant for haematological estimations.

3. If exchange transfusion is indicated, according to the criteria described in Part I, a time within the first nine hours is selected, dependent on the baby's condition.

4. Exchange transfusion is performed by the umbilical route, aiming to achieve 80–90% replacement.

5. The baby is kept in the special nursery for sick babies for a few hours; then, if well enough, he is taken to his mother in the lying-in ward.

6. Haemoglobin estimation, using skin-prick blood, is performed next day and repeated as indicated until discharge from hospital (usually on the tenth day). All babies are seen for examination and haemoglobin estimation at the age of 1 month, and a few need a further test at 6 weeks. This routine is followed in the straightforward case whether the infant has received early exchange transfusion or has been left without early treatment. If the haemoglobin level falls to less than 8.5 g.% during the first six weeks of life a simple scalp-vein transfusion is given.

Blood For Exchange Transfusion

For a baby weighing 8½ lb. (3.9 kg.) or less, two M.R.C. bottles of "bank" blood are required, usually Rh negative and of the same ABO group as the baby.

Compatibility Tests.—Blood is selected on the basis of tests in saline and serial dilutions in albumin, and by the indirect Coombs technique; ideally, both the mother's and the baby's serum are used. When the mother's serum is not available, or in an emergency, Rh-negative blood is used without performing a full compatibility test. In such circumstances we consult the record card to ensure that there is nothing unusual about the maternal antibody.

Age of Blood.—We prefer to use blood no more than three or four days old, but, on occasion, have used blood as old as 20 days without apparent ill effect. That there are advantages in using relatively fresh blood was made clear to us recently. Baby Be, a 5-lb. (2.3-kg.) premature infant with a cord haemoglobin level of 11 g.%, was treated by exchange transfusion at the age of 2½ hours. In spite of this the bilirubin rose, and at 44 hours was 24.7 mg. per 100 ml. A second exchange transfusion was carried out and a bottle of blood from the hospital bank was used. When 230 ml. exchange had been completed the baby suddenly became cyanosed, with grunting respiration, and death occurred almost immediately. At 200 ml. exchange the baby had been very well and the venous pressure 5 cm. As he had tolerated the first exchange well, and as the only unusual feature was that the blood used for the second transfusion was 15 days old, we wondered whether there might be some biochemical explanation. We found that the serum potassium level in the infant at the start of transfusion was 20.8 mg. per 100 ml. and at the time of death 57 mg. per 100 ml. The level in the transfused plasma was 65 mg. per 100 ml., and we therefore attribute this death to cardiac arrest consequent on hyperpotassaemia. This danger has been pointed out by Miller *et al.* (1952).

Hb Content of Blood.—Having been collected into acid citrate dextrose (A.C.D.), bank blood is likely to have a haemoglobin content of only about 11.5 g.%. Therefore, in order to achieve a haemoglobin level of 17 g.% at the end of the transfusion, it is necessary: (*a*) to give the baby considerably more blood than is withdrawn, or (*b*) to adjust the haemoglobin content of the transfused blood to approximately 17 g.% by removing about 200 ml. of plasma from each bottle. This latter method has been our constant practice since the very early days, because we regard overloading of the infant's circulation as a very real danger. Mollison (1951) also recommends using concentrated blood, but Diamond *et al.* (1952) advocate the use of whole blood.

On isolated occasions, when suitable bank blood has not been available, we have called donors, and have preferred to collect the blood into heparin rather than A.C.D., thus minimizing the degree of dilution.

Sex of Donor.—Allen *et al.* (1949) drew attention to the possibility that the sex of the donor might influence the

efficacy of exchange transfusion. In their series of 208 cases, 42 infants received blood from female donors, while 137 received male blood. No deaths occurred in the group treated with female blood, whereas 27 (20%) of those treated with male blood died. They claim that this is a significant difference, and state that it cannot be accounted for on the ground that blood with a high cell volume (and therefore generally from male donors) was purposely used for the most severely affected cases. However, Sacks *et al.* (1950), in their series in which the total mortality was similar to that of Allen *et al.*, found that 12.5% of cases transfused with male blood died, as against 21.8% of those treated with female blood. This suggests that the preferential use of female blood is of doubtful value. It has not been our practice to have the donor blood "sexed" before use, but we have been able to trace the sex of the donors in 158 cases. Fifty-five received male blood, 54 female blood, and 49 blood from both male and female donors. The mortality was the same in the three groups. We have taken account of the donor's sex in 12 fatal cases and in 9 very severely affected infants who survived, but could find nothing to suggest that female blood is superior to male blood. It would therefore seem unnecessary to take account of the sex of the donor when selecting blood for exchange transfusion.

Apparatus For Exchange Transfusion

The following material is required: Cord ligatures; gauze swabs; two transfusion stands; oxygen apparatus; cruciate frame; hot-water bottles; three pairs of small artery forceps; one pair of large scissors; exchange transfusion set; "polythene" catheters of two sizes, internal bore 2 mm. and 1 mm.; two short cannulae to fit tightly within catheters (S.W.G. 10 and 18 respectively); blood for transfusion; blood-collecting bottle containing acid citrate dextrose for waste.

Polythene tubing in 8-in. (20-cm.) lengths is stored in a rubber-stoppered glass tube containing 1% cetrimide and after 24 to 48 hours is sterile and ready for use. The catheter tip is cut square because a pointed catheter is more likely to perforate the vein and produce a false passage. We have found side holes a disadvantage. In 247 of our 250 cases we used a catheter with a 2-mm. bore and a 0.75-mm. wall, especially extruded for us by Messrs. De La Rue. This catheter proved satisfactory even with infants weighing as little as 3 lb. (1.4 kg.) at birth. In two of the three remaining cases only a catheter of 1 mm. bore and 0.25 mm. wall could be passed, while the third was transfused by another route.

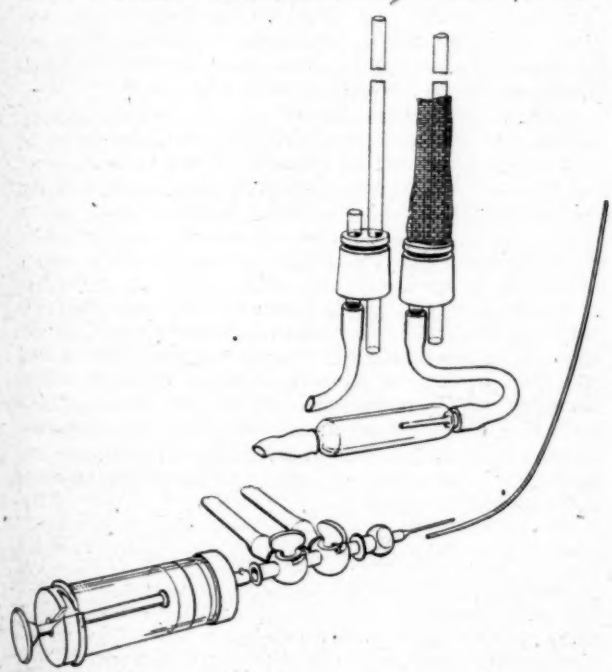

FIG. 3.—Apparatus for exchange transfusion.

Transfusion Set

Many pieces of apparatus for exchange transfusion have been described. Our experience is limited to two—one described by Henderson (1950) but modified to take the larger polythene tubing, and one made for us by Messrs. Baird and Tatlock. This latter set, which we use almost exclusively, is illustrated in Fig. 3. It is very simple, and with the catheter attached the dead space is only 0.5 ml. The essential component consists of two two-way taps machined in one block with large bore throughout, and since it is very light a single operator can use it for long periods, as in the case of two immediately consecutive transfusions. The present pattern is Sima-fitting and made so that a syringe locks on to one end and a cannula on to the other. The locking device is of the pin-slot type, and this sometimes gives rise to air leaks. Therefore we have had a Luer-lock apparatus* made that is otherwise similar to that illustrated. The apparatus is completed by fitting two standard transfusion "giving sets" to the side limbs, but the one intended for waste blood is assembled without either filter or drip-chamber.

We have found "Everett" syringes absolutely satisfactory and prefer the metal-and-glass to the all-glass variety. All-glass syringes tend to stick, because any blood leaking back along the plunger is exposed to the air intermittently and dries. As a lubricant for taps and syringe silicone fluid† is used.

The ease of the operation depends on the use of a large-bore catheter, and, employing 2-mm.-bore tubing, we have not found a Tuöhy adapter necessary. In most cases the same apparatus is used from start to finish without having to disconnect the syringe or wash out any part.

Sterilization.—The apparatus, apart from the catheter, is sterilized by autoclaving and is kept constantly ready for use; the syringes and cannulae in glass tubes, the set and instruments in separate "cellophane" packages.

Route of Transfusion

We normally use the umbilical vein route introduced by Diamond (1948), and, with one exception, our successful experience is limited to this route. We have found it absolutely satisfactory. Wallerstein's (1946) fears that it would be feasible only if a decision regarding transfusion were made before birth have proved unfounded. We disagree with the opinion of Field and Hawkins (1951) that many cases are seen too late for the umbilical vein to be used and that, in any case, it is dangerous because of the manipulations required and the rapid rate of transfusion.

Other routes have been recommended from time to time. The original method (Hart, 1925), also used by Wallerstein (1947, 1948), was that of saphenous or arm vein infusion, combined with the withdrawal of blood from the jugular vein or fontanelle. In our earlier cases we tried this method, but found it technically difficult, and we were able to achieve a satisfactory exchange in only one of the six cases attempted. The method also appeared to involve undue risk of bleeding from the punctured vessels.

We have practically no experience of the saphenous vein and radial artery technique originally used by Polayes and advocated by Wiener and his co-workers (1946, 1949).

No doubt anyone taking enough trouble to master a technique will in the end find it reliable, but the umbilical route, in addition to its technical simplicity, has the following very real advantages: (1) No artificial wound is made; (2) the balance between the volume of blood given and withdrawn can be maintained very accurately or varied at will; (3) venous pressure can readily be measured directly

*Supplied by the Medical Supply Association Ltd., Edinburgh.
†DC 550 Midland Silicones, Ltd.

when a transparent catheter is used; and (4) no important artery is ligated, for, although Field and Hawkins (1951) claim that ligation of the radial artery does no harm, Wallerstein (1948) maintains that there is a risk of ischaemia.

Technique of Transfusion

1. The transfusion is carried out in a warm room, if possible with a temperature of 75 to 80° F. (23.9 to 26.7° C.). The blood is placed in water at 98° F. (36.7° C.) for about 15 minutes before use. The baby, wrapped in gamgee so that only the face and umbilical areas are exposed, is bandaged to the cruciate splint in such a way that no bandages cross the abdomen or chest. A hot-water bottle is placed on each side of the trunk and held in place by a blanket which also forms a hood round the head.

2. Everyone entering the room wears a mask. The operator scrubs up and puts on a sterile gown, while his assistant, usually a nurse, merely washes. She records the amounts of blood exchanged throughout the procedure and notes the time taken for each 100-ml. exchange. She attends to the baby as necessary, including the administration of oxygen if required, and changes the blood bottles when indicated.

3. The cord is swabbed with 1% cetrimide and the baby is covered with a sterile towel, in the centre of which is a small hole. The apparatus is assembled and the blood and waste bottles are suspended from the transfusion stands. By manipulating the taps, blood and A.C.D. in turn are allowed to fill the rubber tubing, thereby expelling all air, while the citrate washes out any blood from the taps.

4. The umbilical cord is divided no more than 2 cm. from the abdominal wall and the stump is brought up through the hole in the towel and packed round with sterile gauze. The vein is readily identified, as it has a larger lumen than the two arteries, which usually lie close together and, because of their thicker walls, tend to protrude from the cut surface. The vein wall is grasped with artery forceps at two points opposite to each other and the closed third forceps is used as a blunt dilator to dilate the vein to a point just beyond the skin margin. A catheter is then introduced gently about 8 to 10 cm. to a point where blood flows freely back along it. If difficulty is experienced at the junction of cord and skin, the cord is gently pulled down in the direction of the pubis and the catheter rotated backwards and forwards, when it will usually pass without difficulty.

5. A direct measurement of the venous pressure can be made by elevating the external part of the catheter and measuring the height of the blood column above the abdominal wall. The measurement can be regarded as satisfactory only if the baby is quiet and relaxed and there is free fluctuation of the blood with respiration. We regard a pressure of less than 10 cm. as normal, but Diamond *et al.* (1952) regard 6 cm. as the upper normal limit.

6. The metal cannula is now inserted into the polythene catheter, attached to the tap unit, and the transfusion begun. 10 ml. of blood is first withdrawn from the baby, and, after turning the appropriate tap, is ejected into the waste bottle. Then 10 ml. of donor blood is taken into the syringe via the other tap, and, with both taps once more in line, is slowly injected into the baby. This cycle is repeated as often as necessary to complete the transfusion, and we aim to take ten minutes for each 100 ml. exchanged. On occasions we have taken as little as six minutes for 100 ml. without apparent ill effect, but too rapid transfusion often distresses the baby. Some experienced workers recommend carrying out the exchange in 20-ml. amounts, but this increases the completeness of the replacement by barely 1%, and we feel that the smaller volume is safer.

From beginning to end the operation takes about 75 minutes, which agrees with the recommendations of Wallerstein (1947), and Diamond *et al.* (1952). It is appreciably shorter than the time recommended by Mollison (1951) and Field and Hawkins (1951).

Difficulties, especially in withdrawing blood, often occur, but can usually be overcome by altering the position of the catheter slightly. Once the best position is found, every effort should be made to keep the catheter absolutely still. Gentle traction on the cord sometimes overcomes difficulties, presumably by straightening out a kink, but we have the impression that excessive traction tends to cause vomiting. The surest way to stop the flow is to suck too hard.

Defects in the apparatus can readily be located by testing it after disconnecting from the catheter.

If desired, additional blood may be given at the end of the exchange, either by the syringe in 10-ml. amounts or by slow drip, the donor set being connected direct to the cannula for this purpose. Unless it is certain that the infant will tolerate additional blood, *none* should be given. If necessary, a simple transfusion given several days later will serve the same purpose with greater safety.

At the end of the operation the cord is ligated in the normal way if long enough. If not, a purse-string suture is used, or a ligature tied round the skin-covered portion of the cord and removed 24 hours later.

Technical Difficulties

Introducing the Polythene Catheter

Difficulty in inserting the catheter can usually be avoided by cutting the cord sufficiently short, so that the remaining vein is not tortuous. It is also important to be sure that the lumen has been entered, for it is easy to make false passages, either alongside the vein or between the coats of the vessel wall. If the catheter has been introduced 8 to 10 cm. and blood has failed to flow, it should be suspected that the catheter is not in the vein. If suction produces only a small amount of yellow fluid this is certain. The remedy is to cut the cord shorter, if necessary flush with the skin, and start again.

Very occasionally the umbilical vein runs an atypical course, and, if varying the line of approach does not succeed, a curved probe can be used to determine the exact path of the vein. In such circumstances the introducing cannula described by Diamond *et al.* (1952) should be of value.

On one occasion we could pass the catheter only about 5 cm. beyond the skin margin, and withdrawal of blood was very difficult. We therefore cut down on the vein above the umbilicus (as described by Pinkus, 1948) and, presumably because of the more direct approach, were able to manipulate the catheter past the obstruction.

If the cord has been tied off short or occluded near the skin margin by means of a metal clip, it should be cut off close to the skin, and no difficulty should be encountered.

In the small number of secondary exchange transfusions that we have performed we have found it satisfactory in most cases to divide the cord close to the skin margin by means of a scalpel. The vein is identified and the catheter introduced in the usual way. Where we have failed with this method we have cut down on the umbilical vein. The technique employed has been to make a transverse incision through the skin about 1 to 2 cm. above the umbilical cord. The skin is then reflected back on to the cord and an aneurysm needle passed behind the cord tissue. This is incised, the vein identified, and the catheter introduced.

Once the catheter is in position the transfusion is conducted as in any other case and technical difficulties are no more frequent.

Maintaining a Satisfactory Flow

Sometimes, even when one is confident that the catheter has been introduced correctly, blood fails to flow or flows only when the catheter is withdrawn a little. This suggests that a clot is present in the vein, and if it cannot be withdrawn through the catheter then the catheter should be carefully withdrawn while gentle suction is applied. It is usually

possible by this means to withdraw the clot, after which a straightforward exchange can be performed. Occasionally parts of the clot may be left behind and cause trouble for the first 30 to 40 ml. Clotting very rarely occurs in the apparatus, but when it does we have found it satisfactory to wash out the taps and cannula with sterile water, followed by saline, then to proceed as usual. Defects in the apparatus and sticking syringes should be rarities, avoided by scrupulous care in their maintenance and preparation. No technical difficulties were encountered in 217 of our 250 "adequate" exchange transfusions. In the remainder the difficulties were as follows: introducing the catheter, 10 cases; clotting in apparatus, 5; leaking apparatus, 4; sticking syringes, 4; maintaining the flow, 10.

General Management

Oxygen Therapy.—Oxygen is not required in the uncomplicated case, but should be available for any baby who becomes cyanosed or distressed. A plastic funnel covering the baby's face is usually satisfactory, but in very ill infants a more efficient method is required. On three occasions the whole procedure has been carried out in an "isolette" incubator, because the infants were premature, grossly anaemic at birth, and showed signs of heart failure. Recently we have used a "perspex" box which fits over the baby and cruciate frame as far down as the groins (Fig. 4).

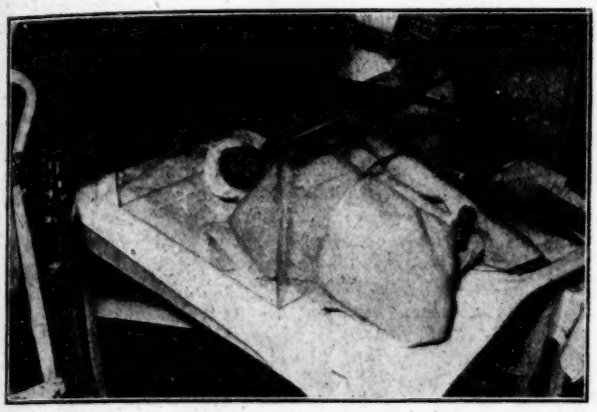

FIG. 4.—Apparatus for oxygen therapy.

By placing two hot-water bottles in the box a temperature of 85° F. (29.4° C.) can be maintained. A concentration of 50 to 60% oxygen is achieved with a flow rate of four litres a minute, and under these conditions the carbon dioxide concentration remains less than 1%. A swinging panel is provided in one wall of the box so that any necessary attention can be given to the baby. Severely affected babies benefit from a period in oxygen both before and after the transfusion.

Use of Calcium.—Theoretically, hypocalcaemia and tetany may be induced when large amounts of blood collected into citrate are used for transfusions of this kind. Therefore many workers (Wallerstein, 1948; Wiener and Wexler, 1949; Diamond *et al.*, 1951, 1952) recommend that calcium gluconate should be given at the end of, or periodically during, every exchange transfusion. We have not investigated this problem biochemically, but clinically have not recognized any signs of tetany. We gave calcium gluconate to four babies whose condition seemed unsatisfactory without any obvious explanation, but were not convinced that it produced improvement in any case. It is possible that, in removing 200 ml. of plasma from the donor blood, we also remove the main excess of citrate, but we have on occasion used whole blood without apparent ill effect.

Use of Heparin.—We have never thought it desirable or found it necessary to use heparin as advocated by Vogel (quoted by Wallerstein, 1947) and Wiener (1946, 1947, 1949).

After-Care

In the straightforward case, the baby's management following exchange transfusion does not differ from that of the normal newborn.

Antibiotics and Chemotherapy.—The prophylactic use of penicillin and sulphadiazine in all cases was recommended by Diamond *et al.* (1951, 1952). At one time 48 hours' penicillin therapy formed part of our routine in a proportion of cases, but as we found that a high percentage of organisms in the hospital concerned were resistant to penicillin we have abandoned this practice. Infection due to exchange transfusion has never occurred in our cases so far as we know. In the occasional case in which infection appears to be a real risk due to an undue amount of manipulation we have preferred to use streptomycin or chloramphenicol prophylactically.

Vitamin K.—This is given intramuscularly at birth as a routine in all cases, and has been continued for five days in many. We feel that this continued administration is not essential. Diamond *et al.* (1952) no longer recommend the use of vitamin K.

Haematinics.—There is no rationale for giving haematinics in this disease.

Breast-Feeding.—We encourage breast-feeding unless there is some other contraindication. Among over 1,000 cases of haemolytic disease we have recognized only two cases of prolonged haemolysis due to transmission of antibody in the mother's milk.

Complications of Exchange Transfusion

Many hazards have been attributed to exchange transfusion, and some apply no matter what route is used, while others concern the use of only one particular method.

Sepsis.—This should be an extremely rare sequel, and we have indicated the steps we take to prevent it in cases exposed to more than average risk. Van Loghem and Bartels (1949) recorded four deaths from infection in their series.

Air Embolism.—Wiener and Wexler (1949) have criticized the umbilical vein route on the grounds that there is a great risk of air embolism. Pickles (1949) and Mollison (1951) also list this as a possible complication. We have never experienced this calamity and consider that the use of a transparent catheter should ensure that no air enters through its lumen. Air could enter the baby by passing up the umbilical vein alongside the catheter, but this can be prevented by tying a ligature round the cord and catheter, or by closing the vein tightly round the catheter by means of an artery forceps. Van Loghem and Bartels (1949) recorded deaths from air embolism, but they elected to use rubber rather than plastic catheters.

Thrombosis of Portal Vein.—Wiener and Wexler (1949) give this as a complication, but it has never happened in our experience.

Perforation of the Umbilical Vein.—This risk, which diminishes with the experience of the operator, is always present. Unless perforation occurs within the abdomen, no serious harm is likely to result. We have made a careful examination of the umbilical vein in all of our fatal cases, but, apart from minimal bruising, have discerned no injury.

Reaction Due to Incompatible Transfusion

Van Loghem and Bartels (1949) reported this as a cause of death in their series, and obviously the risk exists as with any transfusion. We feel that in the newborn, and particularly using exchange transfusion, the dangers are less likely to be serious than in simple transfusion of older subjects. On two occasions we unwittingly used blood which was frankly incompatible.

Case 1.—A baby was given Rh-positive instead of Rh-negative blood by mistake. He pursued an uneventful course; in particular, only mild jaundice, lasting less than one week, developed, and further transfusion was not required. We were able to

demonstrate that the transfused cells were eliminated rapidly although no free antibody was detected in the infant's cord blood.

Case 2.—This was an infant with an Rh-negative mother and an Rh-positive father, but antibodies had not been demonstrated antenatally. The routine cord-blood specimen was Coombs-positive and early jaundice occurred. Exchange transfusion was carried out, using Rh-negative blood of the same ABO group as the baby, but without full compatibility tests. It was later discovered that haemolytic disease was due to ABO incompatibility. This infant also progressed satisfactorily, and, although all transfused cells were eliminated within fourteen days, no additional transfusion was required.

Overloading of the Circulation

This is a very real danger in infants grossly anaemic at birth and one that we encountered early in our experience. A baby admitted from the domiciliary practice of the hospital had a capillary haemoglobin level of 7.3 g.% at seven hours. As his condition remained satisfactory during exchange transfusion, we decided to give an additional 70 ml. of blood slowly at the end of the exchange. The baby became deeply cyanosed and stopped breathing. The catheter was disconnected and blood poured from it, obviously under increased pressure. We allowed bleeding to continue until the pressure was normal. The baby rallied, only to die three hours later, and at necropsy signs of heart failure were found. Because of this early experience we give additional blood only to infants fit at the start and throughout the transfusion, and then never more than 30 to 40 ml. If there is the slightest doubt we do not expose the infant to this risk.

That the possibility of heart failure can never be ignored was once again made clear to us only recently. A baby was born outside and admitted with severe clinical disease. The venous pressure at the start of the transfusion was normal, but, even so, we discarded 10 ml. before carrying out the exchange. At 510 ml. out/500 ml. in, the baby was well and the venous pressure normal. We decided to replace the 10 ml. to complete the transfusion. Having done so, we disconnected the catheter, and simultaneously observed the infant to be deeply cyanosed and the venous pressure to be very high. The removal of 40 ml. of blood, artificial respiration, and the intravenous and intracardiac administration of stimulants were of no avail. The infant died, and at necropsy evidence of heart failure was found. From this we learnt two important lessons: first, 10 ml. of blood is enough to precipitate fatal heart failure, and, second, one should always carefully assess the severity of the case before undertaking treatment. The haemoglobin level at the start of exchange transfusion was only 6 g.%, but unfortunately we did not make this estimation until after the baby was dead.

Before beginning treatment we would recommend that the venous pressure be measured, and, if desired, the manometer described by Mollison (1951) may be used for this purpose. If the pressure is higher than 10 cm. more blood should be withdrawn than is given until the pressure is normal. Most infants with a cord haemoglobin level of 11 g.% (75%) or less appear to benefit by having less blood injected than is withdrawn. As a very rough guide, the negative balance should be about 10 ml. for every 10% of haemoglobin below this level. Whenever the cord haemoglobin is less than 7.4 g.% (50%) we feel that the transfusion should be carried out at a negative balance, even if the venous pressure is within normal limits.

If the venous pressure is high we aim to reduce it as early as possible by removing from the baby 20 ml. of blood and replacing it with 10 ml. This is repeated until the venous pressure is reduced to normal. We regard the high venous pressure as partly compensatory for the anaemia, and consider that the above routine, using blood with a haemoglobin content of about 17 g.%, has the advantage of raising the haemoglobin level at the same time as the venous pressure is reduced. Diamond *et al.* (1952) also use this system, which we suggest is better than the practice of removing 50 ml. of blood from similar cases before injecting any.

Reaction of the Infant to Exchange Transfusion

In about 40% of infants treated by exchange transfusion the general condition deteriorates during transfusion, and in many cases no obvious cause is evident. The risk does not appear to be related in any simple way to the baby's condition at the start, to the birth weight, to the technical difficulties encountered, or to the rate of exchange. Certainly, severely ill babies usually give cause for anxiety throughout the transfusion, but it is not uncommon for an infant with relatively mild disease and in good condition at the start to deteriorate during the transfusion. Collapse is usually due to one of two factors.

(1) *Heart Failure.*—This is usually, but not always, limited to babies grossly anaemic at the start, with a high venous pressure. The main features observed in these cases are cyanosis (readily observed in the lips, but often first noticed because the blood being withdrawn from the baby has become dark in colour), rapid shallow respiration, increased heart rate, and a high venous pressure. The baby, having been active and crying, may become limp and silent or have sighing or grunting respiration with some frothing at the mouth. Oxygen, withdrawal of blood until the venous pressure becomes normal, and slowing the rate of the procedure often result in improvement. If, in spite of this, the baby's condition deteriorates, we would suggest that the transfusion be stopped and the baby placed in an oxygen box. We have done this with benefit in eight instances, and have had no technical difficulty in restarting and completing the transfusion. The catheter is clamped and left *in situ*, and is replaced by a new one when the transfusion is recommenced; alternatively, the cord may be ligated.

(2) *Shock.*—Although some babies show some degree of shock, becoming pale and quiet, with rapid shallow respirations, this is seldom severe enough to cause great anxiety, and they usually recover with warmth and slowing of the transfusion. However, in one or two such infants we have experienced difficulty in withdrawing blood. The giving of 20 to 30 ml. of blood without any being withdrawn resulted in dramatic improvement: the procedure once again became easy and all remained well. But if there is the slightest possibility that the clinical deterioration may be due to heart failure, extra blood should not be given. It is wiser to stop the transfusion, because placing the baby in an oxygen box brings improvement, whichever the cause, and the clinical distinction may be very difficult.

We foresee that full investigation of the biochemical and other factors involved may eventually explain the deterioration in the clinical condition of some of these cases.

Conclusion

We believe that exchange transfusion forms an essential part of the treatment of babies suffering from relatively severe haemolytic disease of the newborn. In practical hands it is a safe and satisfactory procedure. Linked with laboratory prediction beforehand and skilled care afterwards, it should ensure a satisfactory outcome in the great majority of cases.

The cases with which this report is concerned have been collected from a large part of Northumberland and Durham, and but for the good will of the obstetricians, family doctors, and antenatal clinic staffs this material could not have been concentrated in one centre. The Regional Blood Transfusion Centre in Newcastle-upon-Tyne has undertaken the antenatal and cord-blood serological tests necessary for the diagnosis. It is because of the efficiency of this service that such a large proportion of cases have been diagnosed antenatally, and this has materially contributed to the results. As this report deals with cases collected over a period of eight years in the Newcastle-upon-Tyne group of hospitals, it is obviously impossible to mention by name all those to whom we are indebted for help. We would like to thank our medical and nursing colleagues in these hospitals for their continuous help.

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A STUDY OF THE ACTION OF TRICYCLAMOL CHLORIDE

BY

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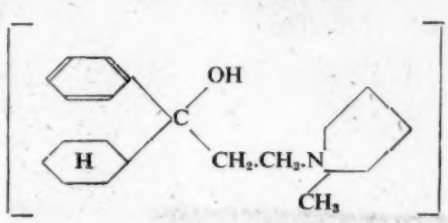
In the search for efficient treatment of gastric and duodenal ulcer the primary object of prolonged reduction of free HCl concentration in the gastric juice has been achieved (Douthwaite and Thorne, 1954). It was postulated that the failure of single large doses of antacids was due to their rapid expulsion from the stomach, especially in cases of duodenal ulceration. Drugs which will reduce the rate of emptying should therefore prolong the antacid effect; at present this is obtainable only by the slow sucking of alkaline or buffering tablets. The difficulty of controlling nocturnal secretion might in this way be overcome.

The belladonna alkaloids and, to a far greater extent, hexamethonium (Douthwaite and Thorne, 1951) by injection, have been used for this purpose.

The object of this communication is to report our experiences with tricyclamol chloride (DL-*N*-methyl-3-*cyclo*hexyl-3-hydroxy-3-phenylpropyl pyrrolidinium chloride), shown in animal experiments to have an antispasmodic and parasympatholytic action. It is an odourless crystalline substance, which is freely soluble in water. It may be given by mouth or by subcutaneous injection. The doses employed have varied from 25 to 100 mg. and are indicated in respect of each experiment.

Our object has been to test the effect on gastric and duodenal motility and tone; the influence on gastric acidity; and the effect of a single dose of antacid on the *p*H of the gastric juice during the action of tricyclamol.



Tricyclamol chloride

Methods

The effects of tricyclamol upon gastric and duodenal motility were observed on the *x*-ray screen during a barium meal and films were taken. Comparison was made with barium meals given without the drug. The influence of tricyclamol on gall-bladder emptying was shown by cholecystography with and without a dose of tricyclamol.

The effect of tricyclamol on the *p*H and levels of free and total acid of test-meal samples were observed and compared with control meal samples obtained without the drug. In three patients tricyclamol was given immediately after passing a Ryle tube—50 mg. intramuscularly in two cases and 50 mg. orally in one case. The meal was eaten and samples of gastric contents were taken every 15 minutes. In a fourth patient 100 mg. of tricyclamol was given orally half an hour before starting the meal.

Two of the patients also received an alkaline mixture (aluminium hydroxide gel *B.P.C.*, 8 ml.) immediately after swallowing the meal. The stomach was not emptied of its resting contents. We wished to discover how effective tricyclamol might be in reducing the acidity of gastric contents under ordinary conditions, since, in actual treatment of peptic ulcer, drugs given to decrease acidity are used in the presence of some secretions still in the stomach. To be of value the drug should reduce acidity in the presence of previously secreted gastric juice.

Three of the four patients were given a "standard breakfast" of one boiled egg, two slices of toast, and two cupfuls of tea. Such a meal allows the response of the stomach to normal food to be measured in terms of *p*H and acidity, and probably represents a more usual gastric stimulus than a gruel meal. It has the disadvantage of not being directly comparable to series of test meals done in the past, when gruel was commonly used for the meal. One of these four patients received a gruel meal.

In an attempt to reduce sampling error (James and Pickering, 1949), about 30 ml. of gastric contents was aspirated at each time. After agitation of the syringe contents, about 7 ml. of the mixture was retained and the remainder returned to the stomach: 5 ml. of each sample was titrated within 24 hours of collection. (Storage at 4° C. before the estimations.) The *p*H was measured electrometrically. Titration to *p*H 3 with 0.5N NaOH solution was taken to represent the level of free acid in the samples. The level of total acid was measured by titration to *p*H 7.

Results

1. *Effect on Gastric and Duodenal Motility and Tone.*—Radiological observation of barium meals showed that gastric, duodenal, and small-intestinal motility and tone were considerably reduced after a dose of tricyclamol. (Figs. 1 and 2 show typical appearances.) Yet in a patient with a partial gastrectomy and symptoms of the "dumping syndrome" emptying of the stomach occurred even more rapidly than usual when 50 mg. of tricyclamol was given intramuscularly before a barium meal. This was associated with extreme flaccidity of the stomach, very well seen on

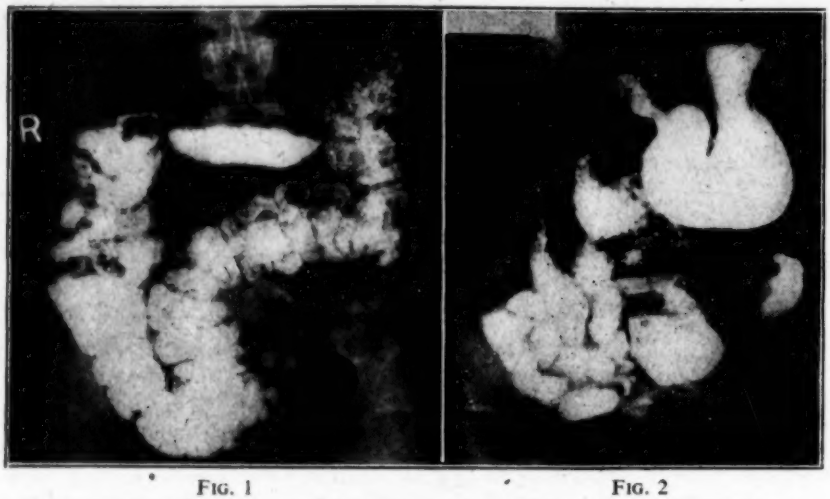


FIG. 1 FIG. 2

FIG. 1.—Control. Four hours after barium meal. FIG. 2.—The same patient as in Fig. 1. Four hours after barium meal. Tricyclamol chloride, 25 mg., was given intramuscularly 20 minutes before the meal.

screening. In a patient in whom a cholecystogram was done the gall-bladder emptied somewhat more slowly after 50 mg. of intramuscular tricyclamol, given half an hour before a fatty meal, than in a control cholecystogram. A little dye could still be seen in the gall-bladder three hours after the fatty meal, while in control films the gall-bladder was empty two hours after the fatty meal.

2. *Influence on Gastric Acidity.*—In two patients, 50 mg. of tricyclamol given intramuscularly produced some rise in *p*H. This effect was short-lived and of relatively small degree. Free acid was again present after one hour in one case and after three-quarters of an hour in the other, a man with a gastro-enterostomy for many years recently complicated by a stomal ulcer. In these two cases intramuscular tricyclamol caused little change in the level of total acid, but there was a slight fall in one of the patients.

3. *Effect of Single Dose of Antacid on pH of Gastric Juice During Action of Tricyclamol.*—Two patients received tricyclamol tablets by mouth. A dose of aluminium hydroxide gel was given as soon as the meal had been eaten. One patient receiving 50 mg. of tricyclamol and 8 ml. of aluminium hydroxide gel showed a moderate rise in *p*H. Free acid was absent for 1¼ hours and then returned in relatively low concentration. There was a smaller fall in total acidity. Another patient was given 100 mg. of tricyclamol by mouth with the additional dose of alkaline mixture. In this case there was a greater rise in *p*H. Free acid was absent for 2¼ hours and then returned and increased in amount. There was a slight reduction in total acidity (see Fig. 3).

Uncomfortable dryness of the mouth, dilated pupils, and blurring of print on reading were noticed in most of the patients. These effects seemed more pronounced after the intramuscular than after the oral use of the drug. In one patient who had 50 mg. of tricyclamol orally no side-effects were observed.

Discussion

Tricyclamol chloride has a marked effect in reducing the motility of the stomach and duodenum, and to a far greater extent than the results produced by hyoscyamine (Douthwaite, 1947). This action may be of value in controlling the pain of peptic ulceration, since it is likely that the pain, at least in part, is due to spasm. Certainly, in the patient with gastro-enterostomy and stomal ulcer, already mentioned, quite severe pain was relieved after repeated oral doses of 50 mg. of the drug.

Tricyclamol has been shown to have some effect in reducing the concentration of free acid in gastric contents after a meal of normal food or gruel. This might be due to diminished secretion of acid juice, or to delay in gastric emptying with a resulting larger volume of gastric contents to dilute gastric secretion, or there might be a combination of both factors.

However, the change in the level of free acid was not marked nor long-lasting when tricyclamol was given alone, and seemed too small to be of much value of itself in the treatment of peptic ulcer. There might be some additional pain-relieving effect due to the association of this factor with the much more powerful spasmolytic action of tricyclamol. Given with an alkaline mixture, tricyclamol potentiated to a certain extent the fall in the level of free acid shown to be due to alkali alone (Douthwaite, 1939). A dose of 100 mg. orally was more effective than 50 mg. Such a combination might assist the process of healing in which free hydrochloric acid is undoubtedly a deterrent factor. It is suggested that a combination of 100 mg. of tricyclamol chloride by mouth with a full dose of antacid might go some way towards overcoming the difficulty hitherto experienced in controlling nocturnal secretion in the treatment of duodenal ulcer.

Although tricyclamol decreased gastric motility, paradoxically gastric emptying became more rapid after giving the drug to a patient with partial gastrectomy. This seemed to be due to the extreme flaccidity of the stomach with greater dependence of the stoma, allowing barium to pour through at a very fast rate. Symptoms of "dumping" were not produced in this patient after taking a barium meal preceded by tricyclamol.

Side-effects sufficient to cause slight discomfort were observed in most of the patients in whom the effects of tricyclamol were studied.

Summary

A preliminary report is presented on the effects of a new parasympathetic blocking drug, tricyclamol chloride.

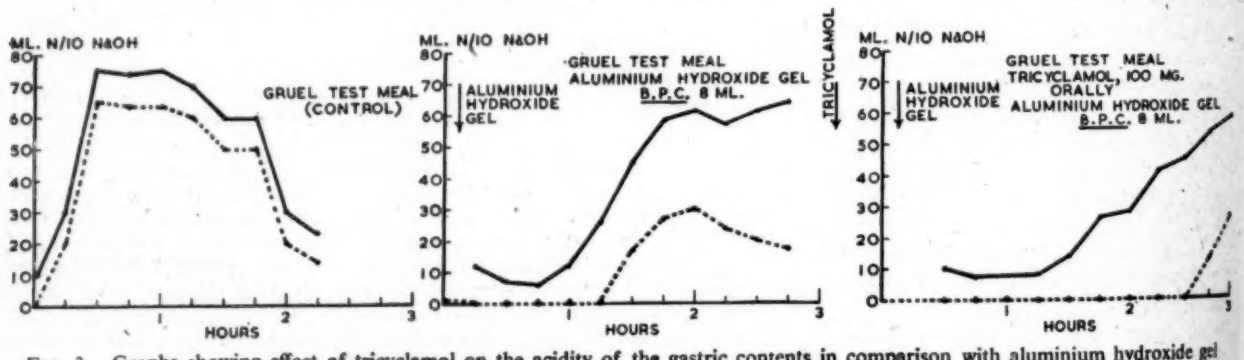


FIG. 3.—Graphs showing effect of tricyclamol on the acidity of the gastric contents in comparison with aluminium hydroxide gel and a control. - - - -, Free acid. ——, Total acid.

The drug had a marked effect in reducing gastric motility and tone.

There was a smaller effect in reducing acidity of the gastric contents.

Tricyclamol prolonged the reduction of gastric acidity obtained by a dose of alkali.

We wish to thank Dr. J. D. Dow for the *x*-ray films, Professor W. R. Spurrell for providing facilities for the analysis of test meals, and Messrs. Burroughs Wellcome and Co. for supplies of the tricyclamol chloride used in these investigations.

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EFFECTS OF VALSALVA'S MANŒUVRE ON THE NORMAL AND FAILING CIRCULATION

BY

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The Valsalva manœuvre (Valsalva, 1707), by producing a rise in intrathoracic pressure, causes an acute decrease in the effective filling pressure of the heart, with consequent changes in the stroke output. An analysis of continuous arterial pressure tracings in the normal subject performing the Valsalva manœuvre has shown that a decrease in pulse pressure occurs when intrathoracic pressure is raised, and that this is followed by a phase of raised diastolic pressure (the "overshoot"). The latter phase has been interpreted as a baroceptor response to the decreased pulse pressure of the former (Sharpey-Schafer, 1953).

Cases of heart failure might be expected to respond to the Valsalva manœuvre in a different manner, since a decrease in effective filling pressure produced by venesection may cause an increase in stroke output (Howarth *et al.*, 1946). Preliminary observations, using continuous arterial pressure records, indicated that this was in fact so (Sharpey-Schafer, 1952).

This paper presents the accumulated data on normal subjects and observations on cases of heart failure of varied aetiology. The results have been interpreted in terms of baroceptor responses to acute changes in pulse pressure.

Material and Methods

Sixty-two subjects with a normal circulation and 63 cases of heart failure were studied. All the cases of heart failure were in sinus rhythm and had a jugular venous pressure raised from 2 to 25 cm. above sternal angle level: 19 were cases of hypertensive heart failure, 9 had ischaemic heart disease, 21 had disease of the mitral or aortic valves, 7 had cor pulmonale (emphysema), 3 severe anaemia, 2 severe thyrotoxicosis, and there was 1 each of the following: primary pulmonary hypertension, pulmonary embolus, haemochromatosis, and chronic myocarditis.

Continuous arterial pressure records were obtained using capacitance manometers (Hansen, 1949), which were also employed for the measurement of intrathoracic pressure (Dornhorst and Leathart, 1952). In some observations a differential manometer system was used (Lee *et al.*, 1954), usually differentiating intra-arterial and intrathoracic pressures.

The Valsalva manœuvre was performed by blowing a mercury column to 40 mm. Hg and maintaining it at that level for about 10 seconds. This was easily accomplished by patients with heart failure, however breathless, and by quite young children for a small monetary reward. The procedure is without risk in heart failure for reasons that will become apparent. All subjects were supine with the trunk raised to 45 degrees with the horizontal.

Results

The difference in response between normal subjects and cases of heart failure was conspicuous (Figs. 1, 2, and 3).

Factors Affecting Response in the Normal Subject

When the intrathoracic pressure is suddenly raised to 40 mm. Hg this pressure is rapidly transmitted to all the arteries and to those veins without valves. The immediate supply pressure to many internal organs, such as the brain, is therefore essentially unaltered. In skin and muscle, however, the venous valves shut and initially the arteriovenous supply pressure is raised by approximately the same amount as the intrathoracic pressure. Since the blood-flow to a part depends on supply pressure and the calibre of the arterioles,

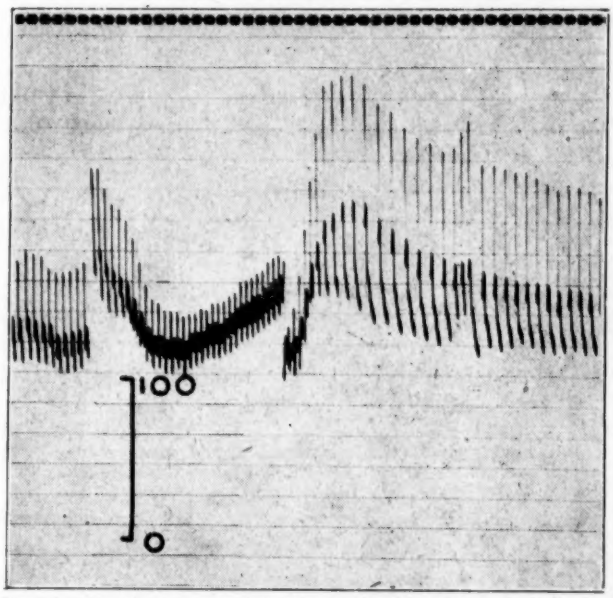

FIG. 1.—Continuous arterial record showing effect of Valsalva manœuvre in normal subject. Calibration in mm. Hg and time marker in seconds in this and subsequent records.

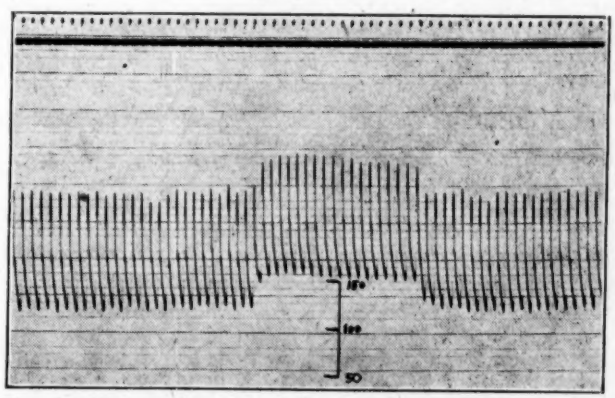

FIG. 2.—Hypertensive heart failure, showing effect of Valsalva manœuvre on arterial blood pressure.

the blood-flow to skin and muscle is initially increased. Thereafter the local venous pressure rises steadily at a rate which depends on previous vasomotor tone, the rise being more rapid in a hot limb than in a cold limb (Fig. 4); as the arteriovenous pressure difference falls the blood-flow to the part decreases. These effects may be seen directly in the capillaries of the nail-bed.

It has already been observed that the accumulation of blood in peripheral veins behind closed valves causes the central effective venous pressure to fall (Lee *et al.*, 1954), with a consequent decrease in stroke output and a fall in arterial mean blood pressure and pulse pressure. The rate at which mean arterial pressure and pulse pressure will decrease depends, therefore, on the initial state of vasomotor tone, being more rapid and considerable in the vasodilated subject. It was shown previously that the rate of fall increased after hyperventilation, which causes vasodilatation of muscle vessels (Howard *et al.*, 1951). The same results have since been found in vasodilatory states produced by indirect heating and by sympathetic blocking agents, and in cases of thyrotoxicosis. It has also been shown that if the rate of accumulation of venous blood in the periphery is decreased by cold or by a pressure suit, then arterial mean pressure and pulse-pressure changes are also decreased.

Under normal environmental conditions the arterial pressure begins to rise again after 5 to 10 seconds, with the onset of peripheral constriction (Sharpey-Schafer, 1953). Simultaneously, there is a decrease or stoppage of blood-flow in the capillaries of the nail-bed.

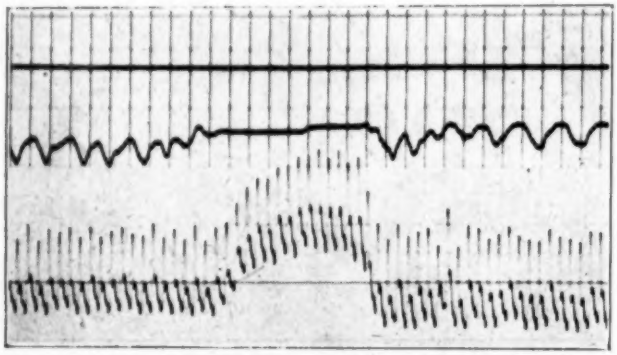

FIG. 3.—Severe hypertensive heart failure, showing increase of pulse pressure during Valsalva manœuvre and decrease of diastolic pressure after release of the raised intrathoracic pressure.

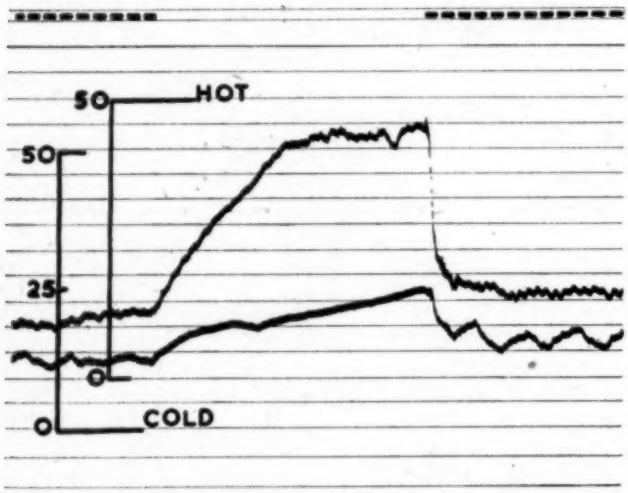

FIG. 4.—Simultaneous venous pressure records from the antecubital veins of both arms of a normal subject. The upper curve is from an arm previously heated; the lower from an arm at a cool environmental temperature. The Valsalva manœuvre is signalled by an interruption of the time marker. The venous pressure rises more rapidly in the heated limb.

The results are summarized in the "normal" part of Fig. 5, in which maximum percentage change in arterial pulse pressure during the phase of raised intrathoracic pressure is plotted against the maximum change in diastolic pressure during the "overshoot." There is a direct relationship in

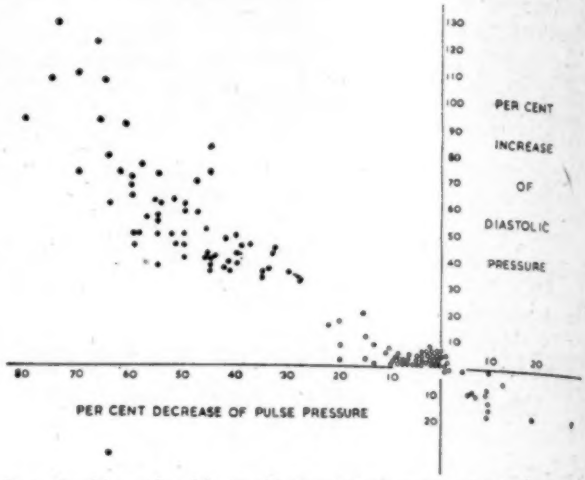

FIG. 5.—Normal subjects—black circles; cases of heart failure—open circles.

$$\text{Percentage decrease of pulse pressure} = \frac{\text{Control pulse pressure} - \text{maximum change in pulse pressure during Valsalva}}{\text{Control pulse pressure}} \times 100$$

$$\text{Percentage increase of diastolic pressure} = \frac{\text{Maximum change in diastolic pressure after Valsalva} - \text{control diastolic pressure}}{\text{Control diastolic pressure}} \times 100$$

the normal subject. In each individual a series of points may be obtained on the "normal" part of the curve by altering the initial vasomotor tone by methods described above.

Response in Heart Failure

The results fall into two groups. In the first, comprising the majority of the cases, there was no measurable change in pulse pressure during the Valsalva manœuvre, and no subsequent "overshoot"; the classical heart-rate changes occurring in normal subjects were also absent (Fig. 2). It would appear, therefore, that in most cases the failing heart is unable to change its stroke volume immediately in response to a rapid fall in filling pressure. Since the pulse pressure remains essentially unaltered, the absence of the "overshoot" is to be expected, if the theory that the latter is due in the normal subject to a decreased pulse pressure is correct. The peripheral constriction in some cases of heart failure must of course modify the response, especially over a short period; but in spite of this an appreciable fall in central venous pressure has been measured.

In the second group of cases there was an increase in pulse pressure during the Valsalva manœuvre, and a subsequent decrease in diastolic pressure, indicating vasodilatation (Fig. 3). It is suggested that these cases, which were clinically the most severe as judged by the height of the venous pressure and course of the illness, were on the falling limb of the Starling filling pressure–output curve, and responded to a decreased filling pressure by an increased stroke output and therefore an increased pulse pressure. The vasodilatation which followed is interpreted as a baroceptor response to the increased pulse pressure, similar to that occurring with other increased pressure transients (Sharpey-Schafer, 1953).

The results are summarized in Fig. 5. In the first group, where no pulse-pressure changes occurred, there was no change subsequently in the diastolic pressure; whereas in the second group the increased pulse pressure was followed by a fall in diastolic pressure, the reverse of the normal.

Discussion

It has been shown previously in animals (Ead *et al.*, 1952) and in man (Sharpey-Schafer, 1953) that increased pressure transients in the circulation give rise to reflex vasodilatation by a baroceptor mechanism. The evidence reported here confirms the theory that, with nervous pathways intact, a decreased pulse pressure produces vasoconstriction and an increased pulse pressure produces vasodilatation. The theory has been shown here to apply not only to the normal but also to the failing circulation. Baroceptor reflexes are active in heart failure provided that the necessary stimulus is applied, as is shown by the cases with increased pulse pressure and subsequent vasodilatation. The lack of baroceptor response in those cases showing no pulse-pressure change is in accordance with this view. Further evidence of baroceptor activity in heart failure in response to pressure changes using other stimuli will be presented elsewhere.

The cases of heart failure reported here were all cases with a raised venous pressure and sinus rhythm. Many other cases of heart disease with a normal venous pressure and patients with abnormal cardiac rhythms have also been investigated, and the results lie on the curve shown in Fig. 5; as might be expected, some are in the normal and some in the pathological part of the graph, with others intermediate in position.

Previous workers (Hamilton *et al.*, 1944; Goldberg *et al.*, 1952; Price and Conner, 1953) have recorded "square wave" patterns on arterial-pressure records in cases of mitral stenosis and occasionally other conditions during the Valsalva manœuvre. The explanations offered have been unsatisfactory, probably because it was not recognized that all forms of heart failure show this phenomenon.

It is of interest that the majority of cases of heart failure did not respond to the acute fall in filling pressure produced during the Valsalva manœuvre by an increased stroke volume, as did the majority of all cases of heart failure studied by the Fick method and venesection (Howarth *et al.*, 1946). The difference in duration of the two sets of observations and the heart-rate changes occurring in the latter group may be sufficient to explain the discrepancy.

Clinical Uses

The main effects of the Valsalva manœuvre may be observed by feeling the pulse in the majority of cases. Rate changes are easily detected, but pulse-pressure changes may also be appreciated. It is usually possible to be certain that the response to the manœuvre is normal by feeling the pulse. Occasionally a spurious "heart failure" response may arise from weak blowing, generally seen in young women who lack the competitive spirit of males and children, or from cheating, which appears to be confined to Royal Air Force personnel who have learned to appose tongue and soft palate, thereby maintaining a mercury column indefinitely without any rise in intrathoracic pressure.

The Valsalva manœuvre may be used to elicit the presence of heart failure in difficult cases and to establish the relative innocence of certain noisy hearts. When used, however, to assess the progress of established cases of heart failure, it shows only too often that little real change has been achieved when they are discharged "compensated" from hospital.

It is also possible by auscultation during the Valsalva manœuvre to decide whether a murmur arises on the right or left side of the heart (Zinsser and Kay, 1950). If the murmur is from the right side it will return immediately on release of the intrathoracic pressure rise; if from the left, a delay of a few beats will be observed. This physical sign is present only if the heart is responding in a normal manner. In most cases of heart failure, since there is no change in stroke output there is no differential accentuation of a murmur. The value of the sign is therefore limited.

Summary

The Valsalva manœuvre causes an acute reduction in the effective filling pressure of the heart and has been used to study the circulation in 62 normal subjects and 63 patients with heart failure. Continuous arterial records showed conspicuous differences in the two groups.

In the normal subjects decrease in arterial-pulse pressure was followed by a rise in diastolic pressure (overshoot). In heart failure from any cause there was usually no change in pulse pressure and no overshoot. In the remaining severe cases the pulse pressure was increased and was followed by a decrease in diastolic pressure.

The results in normal subjects and in heart failure are compatible with the general theory of baroceptor responses to acute pulse-pressure changes. Thus decrease in pulse pressure was followed by vasoconstriction, and increase in pulse pressure by vasodilatation; unchanged pulse-pressure was without effect peripherally.

The Valsalva manœuvre appears to be the simplest repeatable method available at the moment for studying the differences between the normal and failing circulation. It can be used clinically by feeling the pulse.

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VENOUS PULSE IN ATRIAL SEPTAL DEFECT: A CLINICAL SIGN

BY

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The value of observing the venous pulse in the neck is widely recognized, but accurate identification of the waves by timing them against the heart sounds is less commonly practised. This need not be a difficult procedure provided there is no marked tachycardia, particularly where identification of the *a* and *v* waves is concerned, as the former immediately precedes the first heart sound and the latter occurs directly after the second heart sound. Careful observation of the venous pulse in those types of congenital heart disease that predominantly affect the right side of the heart may be of value in establishing the diagnosis. The importance of the large *a* wave in pulmonary stenosis is well recognized (Abrahams and Wood, 1951; Campbell, 1954). It is surprising, therefore, that little attention has been paid to the venous pulse in atrial septal defect. Wood (1950) mentions that it is usually normal, although the venous pressure may be raised in some instances; and Luisada

(1948) states that there may be a very high auricular wave. The purpose of this communication is to describe the pattern of the jugular phlebogram in this condition, and to emphasize that its most important characteristics may be observed by simple inspection of the neck veins.

Material and Methods

Twenty-five patients with atrial septal defect and 16 normal subjects were included in this investigation. Their ages ranged between 3 and 15 years. The diagnosis in the patients with atrial septal defect was made on the accepted clinical and radiographic criteria (Bedford *et al.*, 1941), and all showed incomplete or complete right bundle-branch block on the electrocardiogram (Barber *et al.*, 1950). The diagnosis was confirmed by cardiac catheterization in 19 patients, and in five of these operation for closure was performed and the nature and size of the defect ascertained.

Synchronous jugular phlebograms with phonocardiograms and electrocardiograms as reference tracings have been recorded from each patient. In the majority of cases recordings have been taken on an Elmquist five-channel "klinik" recorder. With this method the venous pulse was usually recorded direct from the internal jugular vein, the pulsations being transmitted to a crystal of Rochelle salt by a fine metal stylus which rests gently on the skin of the neck overlying the vein. In an occasional case the jugular bulb gave a more satisfactory tracing. It was found that certain precautions were necessary to ensure that satisfactory tracings were obtained, and these apply equally to clinical observation of the venous pulse. First, the patient was propped up to about 45 degrees from the horizontal; secondly, the sterno-mastoid was relaxed by keeping his head in the midline; and, lastly, the point of pulsation from which the recording was made was palpated to be sure that there was no superimposed carotid impulse. Tracings were taken with breathing arrested in mid-respiration.

The height of the *v* wave has proved to be of importance in this investigation, and so an attempt has been made to measure this in each individual by comparing it with the height of the *a* wave in the same complex. The height of the *a* wave has been measured from the upstroke denoting the onset of auricular systole to the peak of the wave, and the height of the *v* wave from the point of maximum systolic collapse (*x*) to the peak of the wave. It may be argued that the *v* wave should be measured from the point of pulmonary valve closure rather than from the maximum systolic collapse, as the two do not usually coincide in patients with atrial septal defect. However, the above measurement has been adopted because the large wave observed in the neck following the second heart sound is due to the combined effect of a deep systolic collapse and the large *v* wave itself, and it is with the clinical recognition of this wave in relation to the *a* wave that this investigation is concerned.

Results

So far as could be estimated by cardiac catheterization and by other data, the septal defect was of moderate or large size in all these patients. Five patients were known to have associated pulmonary hypertension, and these are considered separately. No patient was in congestive cardiac failure when the tracings were taken. The 16 subjects with normal hearts were included to demonstrate the normal phlebogram by the methods used in this investigation and to indicate the normal ratio of the size of the *a* wave to that of the *v* wave.

Normal Subjects.—Phlebograms from three of these subjects are shown in Fig. 1. The height of the *a* and *v* waves has been compared in each individual; in six they were of equal amplitude; in three the *v* wave was larger than the *a* wave, but in none was it more than one and a half times as great; in two the *a* wave was slightly larger than the *v* wave, and in five it was up to twice as large.

Atrial Septal Defect.—The level of venous pulsation above the sternal angle was measured in each patient with the trunk at about 45 degrees to the horizontal; in all it was raised, the measurement varying between 2 and 6 cm. The characteristic pattern in those cases uncomplicated by pulmonary hypertension was of a normal *a* and *c* wave, a deep and steep systolic collapse, followed by a tall sharp-rising *v* wave (Fig. 2). In those with pulmonary hypertension proved by cardiac catheterization the size of the *a* wave was increased, and the *v* wave, although still abnormally large, was not as tall as in the uncomplicated cases.

An analysis of these waves has been made in each individual.

The a Wave.—This wave was normal in 17 patients and larger than normal in the five with associated pulmonary hypertension (Fig. 3). The remaining three cases showed either no *a* wave and presystolic collapse or an insignificant *a* wave.

The c Wave.—This was normally registered in all cases.

Systolic Collapse (x).—In 17 out of the 20 cases uncomplicated by pulmonary hypertension the systolic collapse was deeper and steeper than normal. This is clearly shown in Case 2 of Fig. 2.

The v Wave.—In all the 20 cases without pulmonary hypertension the *v* wave was taller than normal and tended to rise sharply to a peak immediately after the abnormally deep systolic collapse; following pulmonary valve closure (Fig. 2) the steepness of this ascending limb was further accentuated in many cases. The height of this wave has been compared with the *a* wave in these patients; it has been termed "normal" if it was slightly greater than, equal to, or smaller than the *a* wave; "large" if it was one and a half to three times as large as the *a* wave; and "giant" if it was more than three times as large as the *a* wave. By these criteria the *v* wave was giant in seven patients and large in thirteen. In three instances it was eight times the height of the *a* wave.

In all but one of the five patients with pulmonary hypertension the *v* wave was also larger than normal, but this change was less

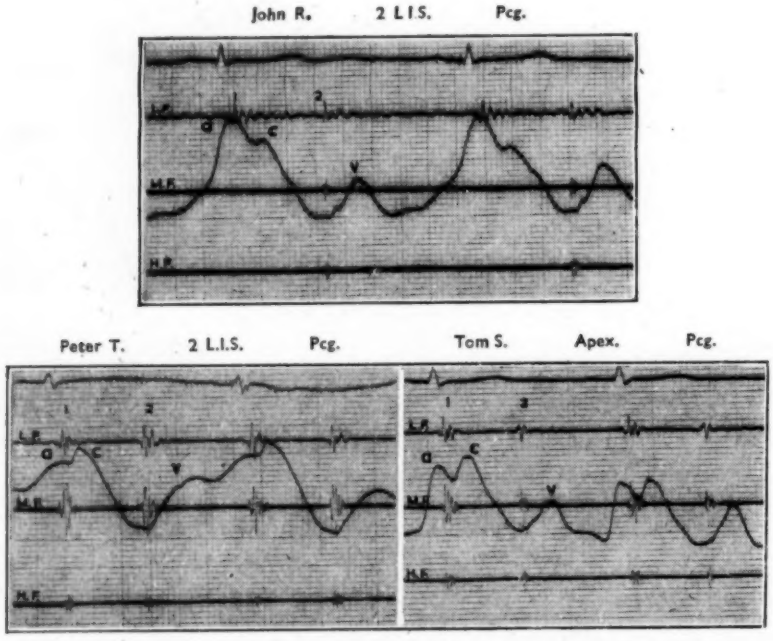

FIG. 1.—Jugular phlebogram in three normal children. 2 L.I.S. = Second left intercostal space. Pcg = Phonocardiogram. L.F. = Low frequency. M.F. = Medium frequency. H.F. = High frequency. 1 = 1st heart sound. 2 = 2nd heart sound.

marked than in the uncomplicated cases. Because the *a* wave was also of increased amplitude in these patients, the height of the *v* wave could not be profitably compared with it.

Diastolic Collapse.—The diastolic collapse was well marked in most patients. In two cases in which no *a* wave was recorded it was continuous with the presystolic collapse.

Discussion

A raised venous pressure with an abnormally large *v* wave has been shown to occur in 20 children with atrial septal defect. This wave is usually sharply defined and can be seen on inspection of the neck veins and identified from the *a* wave by its relationship to the second heart sound. Its differentiation from a large *a* wave helps to distinguish this condition from pulmonary stenosis. We have found a large *a* wave in some mild and moderate cases of the latter as well as in more severe cases; and it is these lesser degrees of pulmonary stenosis that may be confused with atrial septal defect because of the occurrence of a widely split pulmonary second sound in both conditions (Leatham, 1954; Bonham-Carter *et al.*, 1954).

The finding of a large *a* wave in a patient suspected of having an atrial septal defect or the development of such a wave in a known case over the course of time suggests the presence of pulmonary hypertension.

The larger wave following the second heart sound in these patients is probably caused by two separate factors. The deep and steep systolic collapse that is often present is thought to be due to a hyperdynamic right ventricle causing an exaggerated descent of the auriculo-ventricular septum. Following maximal systolic ejection there is a rebound of this septum into the cavity of the right auricle, and the height of the sharply rising wave so produced is then accentuated following pulmonary valve closure by overfilling of the right auricle from the left auricle through the septal defect. Immediately the tricuspid valve opens at the end of the second heart sound there is a sharp fall in pressure in the auricle as blood enters the ventricle, and a steep diastolic collapse wave is produced.

Ratio of Height of v Wave to a Wave in Normal Subjects and in Children with Atrial Septal Defect

Ratio of *v* Wave to *a* Wave *v* : *a*	Classification of *v* Wave	Normal Subjects	Atrial Septal Defect (Without Pulmonary Hypertension)
1 : 2	Normal	5	0
1 : <2	Normal	2	0
1 : 1	Normal	6	0
1·5 : 1	Normal	3	0
1·5–3 : 1	Large	0	13
>3 : 1	Giant	0	7
Total		16	20

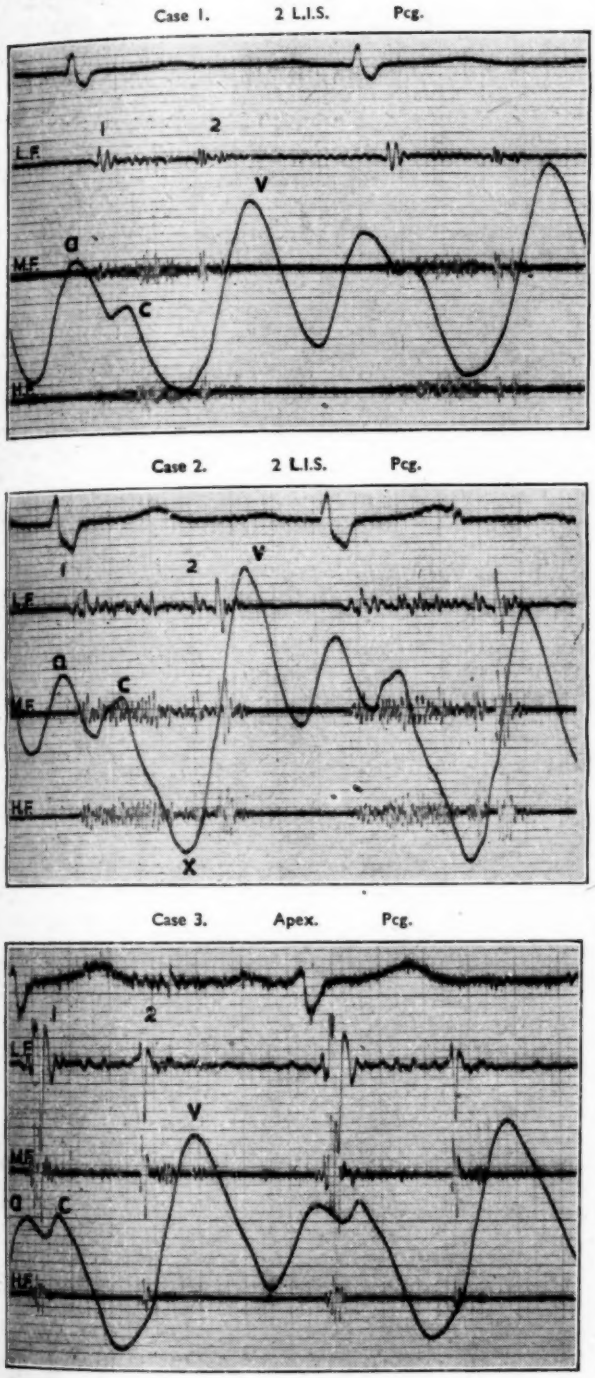

FIG. 2.—Jugular phlebogram in three patients with uncomplicated atrial septal defect. X = Systolic collapse.

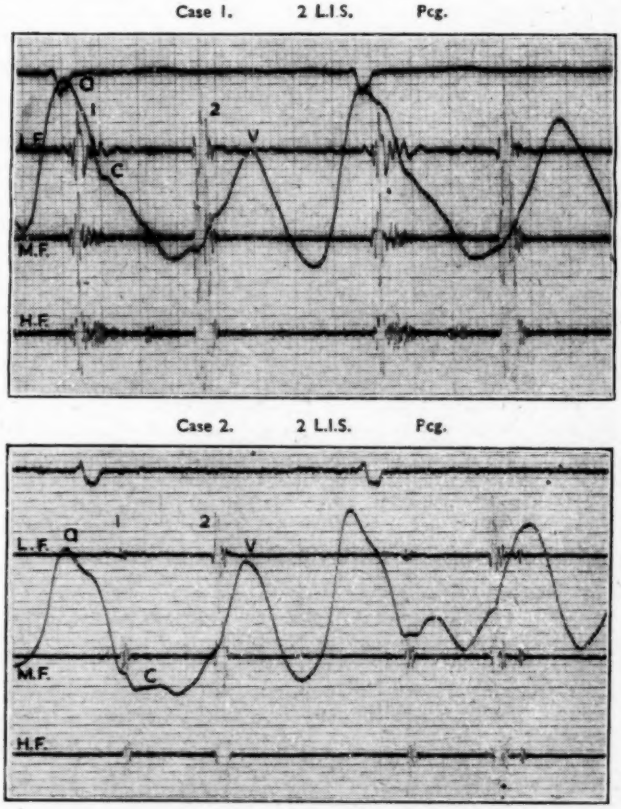

FIG. 3.—Jugular phlebogram in two patients with atrial septal defect and pulmonary hypertension, proved by cardiac catheterization.

The large *a* wave preceding the first heart sound in those cases complicated by pulmonary hypertension is probably caused in a similar way to that found in pulmonary stenosis (Laubry and Pezzi, 1913). As a result of peripheral pulmonary vascular resistance right ventricular hypertension occurs, and this then constitutes an obstruction to auricular systolic ejection, which in turn produces increased auricular systolic contraction and a large *a* wave in the venous pulse.

Summary

Inspection of the neck veins in children with atrial septal defect reveals a raised venous pressure and exaggeration of one of the waves of the venous pulse. Simultaneous auscultation identifies this large wave, by its time relationship to the second heart sound, as the *v* wave. When pulmonary hypertension is present in these patients the *a* wave also becomes larger than normal.

Recordings of the venous pulse in 25 patients with atrial septal defect compared with those of 16 normal children have confirmed these findings. They have also shown that there is exaggeration of normal systolic collapse in these patients, and this contributes to the prominence of the large *v* wave.

An attempt has been made to explain the haemodynamics of these changes in the venous pulse.

It is believed that the large *v* wave in atrial septal defect is a useful clinical sign, particularly in differentiating this condition from pulmonary stenosis.

I am indebted to Dr. Alexander Nadas for permission to include eight patients in this investigation who were seen at the Children's Hospital, Boston, Mass., and who have been mentioned in a previous communication (Reinhold and Nadas, 1954). I am also indebted to Dr. R. E. Bonham-Carter for his constant help and encouragement during this investigation and to Drs. J. F. Goodwin, C. H. M. Walker, M. G. Thorne, and J. P. M. Tizard for their constructive criticism of this paper. Mr. G. H. Bryant gave valuable assistance in helping to obtain the recordings.

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Writing in the *Scientific American* (February, 1955) on "A Study of the Anti-scientific Attitude," Bernard and Judith Mausner (respectively a social psychologist and a physician) ask: "Can scientists draw any lessons from the anti-fluoridation outbreaks?" These writers attribute the strength of the opposition to the fluoridation of water supplies to three main factors. "Firstly, the anti-fluoridation arguments are understandable, easy to follow. Their weaknesses are often difficult for a layman to grasp. Secondly, these arguments are grounded in some of the most widely held ideas and emotions of our culture. In their appeal to respect for individual rights, to fear of poison, to a watchful conservation of public funds, they ring a bell for most people. Thirdly, they are clearly related to the *Zeitgeist*, the current suspicion of scientists, the fear of conspiracy, the tendency to perceive the world as menacing. In contrast, the proponents of fluoridation have all too often ignored public psychology in presenting their case. They have relied too heavily on the fiat of organized science, and have tended to dismiss opponents as 'crackpots' and to deride their arguments. The greatest flaw has been the failure to prepare the public adequately. As a result there develops a polarization of attitudes which makes it very difficult to change opinion."

FRACTURES OF NECK OF FEMUR

INCIDENCE AND IMPLICATIONS

BY

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This investigation is concerned in assessing current and future problems in the organization of treatment for fractures of the neck of the femur.

In June, 1952, a fracture and orthopaedic unit was opened in the Royal Infirmary, Dundee, to which all fractures in the city and environs are referred. This survey has been made in the belief that the 190 cases encountered in the two years completed are the total incidence and unselected. The technical details of treatment and results have not been considered except in so far as they bear on principles involved.

The series is thought to be unselected for the following reasons: (1) The region is small and the fracture and orthopaedic service complete. Fractures are no longer treated in the general surgical wards of the teaching or other hospitals. (2) All such cases are treated in a 66-bed unit in the teaching hospital, which is associated with a 280-bed country orthopaedic hospital carrying out most of the interval orthopaedic treatment for the region. (3) No recent fracture of the neck of the femur from Dundee or the environs was treated in the country hospital. (4) No case was refused admission for any reason whatsoever. (5) The small number of nursing-home cases has been included.

Classification

Study of the age incidence shows a clearly defined distribution, as is apparent in Table I. It seemed significant that two female patients under 50 had had violent falls at work, while none over 50 had. In the men, however, major accidents are equally scattered over the normal life-span. The average age of the male patients is lower, as shown in Table II. The average for the female patients of 75 years is higher than in previous series (Stebbing, 1927, 69 years; Watson-Jones, 1935, 60 years; Murray and Frew, 1949, 62 years). This bears out the unselected nature of the series and, presumably, the significance of the ageing trend of population distribution. The source of the classical fractures of the upper end of the femur is thus determined by age.

TABLE I.—*Pattern of Incidence (Female): City of Dundee Census Area*

Age (Years)	Cases, 1952–3	Cases, 1953–4
Under 50	0	0
50–54	1	1
55–59	4	1
60–64	3	3
65–69	7	3
70–74	11	13
75–79	8	10
80–84	10	8
85–89	3	7
90–	1	3
Total	48	49

TABLE II.—*Average Age (190 Cases)*

Sex	Fracture Type	Average Age	Cases in 2 Years
Male	Cervical	66·8	14
,,	Trochanteric	65·5	36
Female	Cervical	75·8	67
,,	Trochanteric	75·4	73

The further classification of the cases as cervical or trochanteric fractures follows the accepted anatomical and prognostic points of differentiation.

Inferences from the Survey

For the reasons stated it has been found possible not only to analyse accurately the problems in management and disposal but also to relate the cases to the known population at risk. The figures thus obtained are thought to give the first accurate estimate of the incidence of these injuries. Of the 190 cases recorded, 130 arose in the districts included in the population census for the city of Dundee in 1951. The latter alone have been considered in calculating fracture rates per 100,000 population of like age and sex. It was impossible to relate the country cases to the rural population: some patients from outlying districts go to hospitals in other regions. This group of cases has been included only in analysing management and disposal.

Finally, the fracture rates have been applied to the projected population estimates for 1965 and 1975, with a view to determining the effect of the expected change in distribution by age of the population, and this is shown in Table III. The calculation has not been presented for male cases.

TABLE III.—*Total Incidence (Female)*

Age Group (Years)	1952-3		1965		1975	
	Population at Risk	Annual Cases	Projected Population	Expected Cases	Projected Population	Expected Cases
50-54	6,393	1	6,300	1	6,500	1
55-59	5,494	2	6,400	3	5,400	2
60-64	4,864	3	5,900	4	5,700	4
65-69	4,191	5	5,200	6	5,400	6
70-74	3,327	12	3,900	14	4,500	16
75-79	2,416	9	2,800	10	3,400	13
80-84	1,136	9	1,700	13	2,000	16
85-	513	7	900	12	1,000	14
Totals		48		63		72

It is difficult to distinguish the classical fractures of elderly men from those due to violent accident. It is for the same reason that the annual male incidence is variable as compared with the regular, annual, and inevitable group of female cases.

Incidence

The two yearly totals of female cases did not differ; and the distribution followed such an orderly pattern that the picture does not appear to have been distorted by any gross inaccuracy (Table I). The cases from the specified area, and not resulting from major trauma, have been related to the population at risk. Fracture rates per 100,000 of each age group have thus been calculated on the basis of the average annual admissions. It is clear, with the continuing trend towards a greater proportion of elderly people, that the incidence of these fractures must increase. This increase has been estimated on the Registrar-General's projected population tables. The estimate is probably conservative, as it appears that the risk of this injury increases greatly with age.

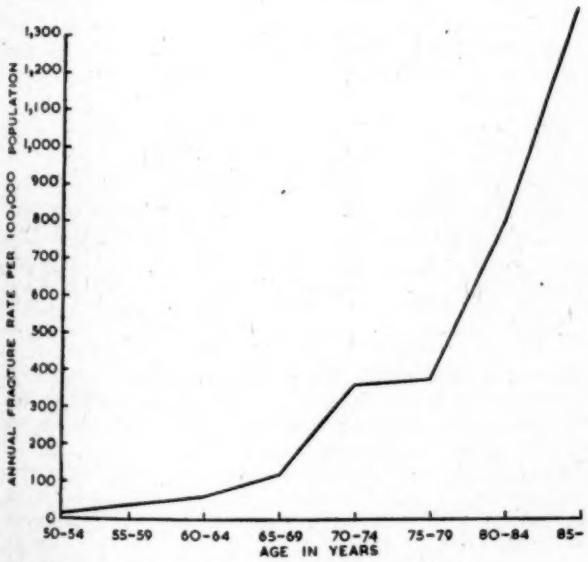

FIG. 1.—Risk of injury (females).

A graph showing this increasing risk is produced when the fracture rates are plotted against the age groups to which they apply (Fig. 1). Thus, not only will there be more elderly people at risk, but their average age, by being higher, will fall in an age group even more prone to these injuries. Since the incident of fracture is related to the senile state of the bone rather than to a particular mechanism, these cases must always occur. Accordingly the tendency to house ever more elderly people in institutions is in itself no safeguard. Indeed, four cases in this series came from such institutions. This is in agreement with the finding that the commonest single accident of those thus injured at home was a fall at the bedside.

The annual number of such fractures is important in planning an accident service. The cases in this series constituted 7% of the male and 20% of the female admissions.

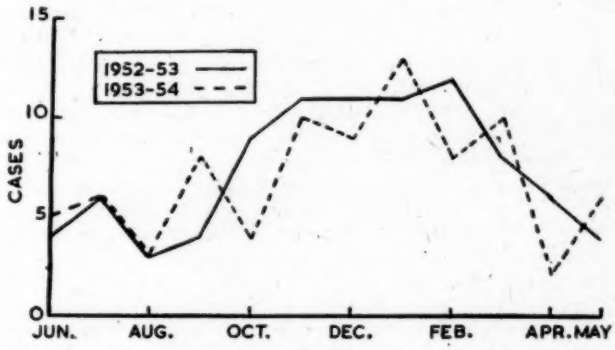

FIG. 2.—Seasonal incidence (females).

The fuller implication of this is to be found in analysis of the actual stay in hospital. Even when 78% of cases were treated operatively the average duration of stay was a few days more than that of all the other types of cases. The female cases actually occupied 22% of the bed-days for their ward in a year.

A seasonal increase in incidence was found to be a reality, as shown in Fig. 2. The explanation of this is not clear. In two consecutive wintry weeks in which came the highest number, no patient was injured in a fall out of doors. Most probably the physical integrity of elderly people is so delicately balanced that the slightest indisposition can upset it. On the other hand, the gale of 1953 which caused so many national disasters blew over three old people in the street, thus increasing the incidence for that month by 50% in a single blast.

Implications

Certain general observations on management seemed relevant to the organization of treatment.

1. Two methods of operative treatment were used. The standard operation was the insertion of a stainless-steel Smith-Petersen nail of the King type or of a similar nail bolted to a McLaughlin plate. Standardization of procedures in this way obviates the necessity for a multiplicity of internal fixation appliances and instruments related thereto. It also familiarizes the surgical and nursing team with the method. This surgical technique had an interesting sequel in one case. The patient first had a cervical fracture nailed. One year later, while freely ambulant, she sustained a

trochanteric stress fracture. This was successfully treated by bolting a plate to the nail already in position. Only two cases were treated by other surgical means.

2. No matter how skilful or experienced the surgeon, the insertion of a nail-plate and screws requires so many separate actions that the minimum time taken is considerable. The insertion of a Smith-Petersen nail alone is delayed only by difficulties in reduction or radiography. The introduction of such advances as xeroradiography will be a matter of importance in reducing the time taken. The hours spent on fractures of the femoral neck give some index to the number of surgeons, anaesthetists, and other staff required to meet the inevitable increase in cases.

3. The patients in this series were treated by a group of surgeons with similar views favouring early operative intervention. Thereafter, immediate mobilization was encouraged by the nursing and physiotherapist staff; no weight-bearing was allowed for approximately three months, at which time walking was recommenced with crutches. Operation was performed on 78% of the patients; only one died within twenty-four hours of operation and none during it. Forty-four patients were treated otherwise. Incidental medical conditions were the contraindication on 26 occasions. The length of time since injury was a reason 15 times. Other reasons were: undisplaced trochanteric fractures, 5; grossly comminuted and technically subtrochanteric fractures, 5; refused operation, 2; suitable internal fixation material not available, 2; trochanteric fracture, opposite leg short, 1.

4. The assessment of the patient's general condition was frequently time-consuming. The 190 patients presented a total of 151 significant pathological states. No less than 58% were discovered to have one or more incidental medical conditions of such severity as to influence decisions on treatment and prognosis. In the making of these decisions much help was given by the anaesthetists and physicians, who, as the series progressed, found noticeably fewer absolute contraindications to what were often regarded as life-saving operations. It is difficult to decide at which stage a patient with chronic exudative bronchitis will fare worse from surgery than from the restrictions associated with anything short of superlative non-operative measures. Deaths from chest complications in patients known to be bronchitic were, as expected, less common after nailing than during traction. In this connexion, too, difficulty was encountered in deciding the primary cause of death in fatalities. The cause given was found to vary more with the individual house officer than with any other consistent factor. Frequently it was no easier for the senior staff to decide.

5. The patient's general condition often appeared to improve for at least the first twelve hours after admission. After that, the opportunity for surgery, if not soon taken, seemed lost. This physical reaction, whether due to stress and its subsequent exhaustion or not, was paralleled in the mental reactions.

6. It rarely seemed necessary to intervene within hours of the accident; and such routine early operating could lead too readily to a reputation for ruthlessness which might not be entirely unfounded.

7. There were on average three of these operations a fortnight, each occupying one to one and a half hours' theatre time. A considerable load could thus be placed on the night staff if emergency reduction and internal fixation were routine. This was, however, sometimes done. One session included four cases. Accordingly, 76% were carried out within 24 hours and 93% within 48 hours of admission; 70% of the patients had been admitted within 24 hours of fracture.

8. The later ward management demands attentions other than the all-important one of devoted nursing. The proportion of elderly patients, when high, has a deleterious effect on ward morale. This is due largely to the nocturnal disturbances of those disorientated by senile cerebral ischaemia. In the series no fewer than 9% had cerebral arteriosclerosis to the point of having had a catastrophe resulting in paresis; a greater number were disorientated. This aspect of ward management has already had deserved publicity with regard to the nursing of adolescents (Stuart-Clark, 1953). The sounds associated with the inevitable deaths and the utterances of the senile arteriosclerotic dements are not for young ears. It appears, therefore, that some form of segregation is necessary. In view of the expected large total increased incidence it seems probable that the answer will be found in total segregation of the female cases in special accommodation.

9. The high percentage returned to normal is discussed under the heading of disposal of the patients. This factor alone would supply an incentive to those nursing cases of fracture of the neck of the femur which is not enjoyed in geriatric wards. Further, this branch of nursing is a specialized matter which segregation would facilitate.

Disposal

In recent years much has been said of the difficulties in discharging elderly patients from hospital. Here, considerable help was forthcoming from patients' relatives, friends, and general practitioners, as shown by the disposal of 114 patients (Table IV). Of those who went home, 16 had previously lived alone. They spent an average of 46 days in hospital, a time not greatly beyond the general average.

TABLE IV.—*Disposal of* 114 *Patients*

Discharged to own home or to relatives or friends		80·7%
Discharged to the geriatric unit		12·3%
Previously lived alone	7	
Previously lived with someone	5	
Previously lived in institution for elderly	1	
Originally admitted from geriatric unit	1	
Discharged to nursing-home, cottage or other hospital		7·0%

In this series, in which mortality was high and morbidity low, the main problem was not one of the institutional disposal of an invalid, but of the delay in gaining access to the care of a relative for rehabilitation, whether the patient lived alone or not (Ferguson and MacPhail, 1954). It was noted, however, that some aged patients progressed less well after return home, for no other apparent reason than that discharge from hospital removed the only remaining incentive to the will to live.

Results

It is appreciated that results of treatment cannot be assessed at this stage. The comment, however, seems justified that, on a short-term basis, morbidity was low.

The mortality figures at the end of the two-year period are shown in Table V. The high mortality rate for trochanteric fractures in women needs explanation. In the first instance

TABLE V.—*Mortality* (190 *Cases*). *Overall Mortality* = 31.6%

Sex	Fracture Type	Operative Treatment		Conservative Treatment	
		No.	Deaths	No.	Deaths
Male	Cervical	12	5	2	1
,,	Trochanteric	21	7	15	3
Female	Cervical	61	16	6	3
,,	Trochanteric	52	20	21	5

a high overall mortality reflects the veracity of the unselected nature of the series. The 52 operation cases presented with a total of 41 serious incidental medical conditions, whereas the 21 treated without operation presented with only six serious incidentals. The explanation for this is that the majority of the cases treated conservatively happened to be so treated for reasons not likely to affect the prognosis adversely—namely, undue time from fracture till admission, gross comminution, lack of suitable internal fixation

apparatus, or patients' refusal to avail themselves of surgery. Finally, no death occurred in this group other than among those treated conservatively because of some serious incidental condition.

Summary

The total incidence of fractures of the femoral neck during two years is analysed.

The inevitable increase in incidence, which is applicable generally, is calculated.

Additional staff and accommodation will probably be required for this contingency.

The suggested segregation of female patients is discussed.

Problems in treatment and disposal are outlined.

I am indebted to Mr. I. S. Smillie, surgeon in charge, Eastern Region (Scotland) Orthopaedic Service, for much encouragement and constructive criticism; also to the surgical and secretarial staff for all their help.

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SULPHAEMOGLOBINAEMIA

A REPORT OF FIVE CASES

BY

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Cyanosis in warm skin, in the absence of obvious disease of the cardiovascular and respiratory systems and of polycythaemia, calls for spectroscopic examination of the blood, and in a proportion of such instances either methaemoglobin or sulphaemoglobin, or both, may be identified.

Methaemoglobin consists of oxidized haem linked to native globin, and is present in traces in normal erythrocytes, in which an enzyme system constantly reduces any methaemoglobin. This enzyme system is probably defective in congenital methaemoglobinaemia. Sulphaemoglobin, in contrast, is invariably a pathological product. Its exact chemical constitution is unknown, but it is thought that a sulphur atom has been incorporated in the pyrrole components of the haem molecule and that the mode of linkage of the haem to the globin moiety is altered. There is no intracellular mechanism for the reconversion of sulphaemoglobin to haemoglobin, nor can reconversion be effected by any known drugs. Sulphaemoglobin remains in the erythrocyte, an irreversible product of haemoglobin metabolism and a harmless though inert pigment, until the cell is destroyed, and there is no evidence that the formation or retention of sulphaemoglobin shortens the average life span of the cell. The only ill effect that can be attributed to it is anoxia, due to the immobilization of oxygen-carrying haemoglobin in the form of an inert pigment.

Both pigments are identified by the presence of an absorption band in the red part of the light spectrum—the methaemoglobin band at 625–655 millimicrons, and the sulphaemoglobin band at 615–630 millimicrons. The absorption band of methaemoglobin is dispelled when a few drops of 5% potassium cyanide are added to the laked blood. This procedure leaves the absorption band of sulphaemoglobin unchanged, but it disappears on adding hydrogen peroxide alone.

In the human subject sulphaemoglobinaemia may follow the ingestion of compounds belonging to two groups: (1) nitrogen-containing compounds such as potassium nitrate, sodium nitrite, or nitroglycerin; and (2) aromatic amino-compounds, such as the sulphonamides or the aniline derivatives acetanilide and phenacetin.

Many cases of sulphaemoglobinaemia due to drugs have been reported in recent years, and the following five patients present few new features, but several aspects of their histories merit discussion.

Case 1

A spinster aged 70 came into hospital on October 26, 1951, complaining of feverishness and of pain in the right iliac fossa and in the back for two weeks. She was accustomed to taking saline aperients regularly, and her bowels were more constipated than usually. She had taken only a few aspirin tablets for the pain.

She was febrile, pale, ill, and not cyanosed. The fingers were clubbed. A blood count showed: Hb, 11.9 g.% (Sahli); red cells, 3,860,000 per c.mm.; P.C.V., 40%; M.C.V., 104 cubic microns; M.C.H.C., 29.75%; white cells, 9,200 per c.mm.; E.S.R., 73 mm. in one hour (Westergren). The urine showed a trace of albumin, no excess of urobilin, and no other abnormality. Clinical and radiological examination suggested a resolving pneumonia, and acute osteomyelitis of vertebrae D 12 and L 1 was diagnosed later. Both conditions resolved with antibiotics.

Aspirin was prescribed for her pain. On October 31 she was cyanosed, and spectroscopic examination of the blood showed a well-marked band in the red due to sulphaemoglobin. On December 17 sulphaemoglobin was still present in a 1 in 20 dilution of blood, examined in a 1 in. (2.5 cm.) thickness. On January 7, 1952, during chloramphenicol therapy, the patient developed loose stools from which type-specific *Bact. coli* (beta type) was grown. The diarrhoea stopped on January 16, and five days later no sulphaemoglobin was detected in a 1 in 5 dilution of blood. The patient went home on March 5.

She was readmitted in October, 1952, with gastric carcinoma. There was no cyanosis, and no sulphaemoglobin was detected.

Case 2

A widow aged 66 had suffered from a duodenal ulcer for 16 years, and was admitted on October 12, 1953, following a haematemesis. She had been subject to headaches most of her life, and had taken an occasional "askit" powder to relieve them. For a year her headache had been very severe and persistent, and her weekly consumption of powders had been two to three dozen. At night she took two compound codeine tablets. For 16 years she had regularly taken a powder thrice daily after meals, which was prescribed by her doctor to prevent her ulcer pain and to keep her bowels regular. For six to seven months she had had paraesthesiae of the hands and feet.

On admission she was slightly cyanosed. The haemoglobin was 4.2 g.% and R.B.C. 2,070,000 per c.mm. The urine showed green to Benedict's solution; no albumin or excessive urobilin. Next day sulphaemoglobin was detected in a 1 in 75 dilution of blood. Its concentration slowly declined, and on December 3 it was detectable only in 1 in 20.

A barium-meal examination on November 17 showed an ulcer deformity of the duodenal cap but no crater. The patient improved slowly, but the blood urea was constantly raised. Pyuria occurred in late October, and it was thought that renal function was impaired by chronic pyelonephritis. The patient returned home on December 29.

She was readmitted on June 9, 1954, following a further haematemesis. Her headaches had persisted but she had taken only aspirin for them, as instructed. She was not cyanosed, and no sulphaemoglobin was detected.

Case 3

A married woman aged 49 was admitted on March 18, 1954, for restabilization of diabetes mellitus, which she had had for four years. She had occasional headaches, and for six months had had paraesthesiae of the feet and legs. For about three months she had had pruritus vulvae with ulceration. For many months she had taken two or three askit powders a day, not to relieve pain but for their "tonic effect."

She was pale and not cyanosed. The haemoglobin was 9 g.%, R.B.C. 4,100,000 per c.mm., and W.B.C. 19,200 per c.mm. The blood was examined spectroscopically on account of the history of regular consumption of powders, and sulphaemoglobin was present. It was still detectable on April 6 in blood diluted 1 in 7.

Case 4

This patient, a woman aged 58, separated from her husband in 1936, had no children, and lived alone. She had a history of psoriasis in childhood, and of three "nervous breakdowns." She had recurrent varicose ulceration, and dressed the ulcers herself, but had neglected them recently. She had taken askit powders regularly for two years, usually three or four a day, but at times nine or ten. She had been accustomed to taking one for occasional headaches all her life, but in the past two years she took them not so much to relieve pain as to "buck her up" if she felt depressed. For several years her face had been puffy.

She was admitted on March 12, 1954, because of post-"influenzal" asthenia and constipation. She was cyanosed, dyspnoeic, and extremely weak, and had a puffy "moon face." The signs of congestive cardiac failure were present, and gravitational ulcers almost encircled the lower thirds of the legs. The pulse rate was 100; B.P. 120/50 mm. Hg. Crepitations were heard at the lung bases; knee- and ankle-jerks were absent. The anal sphincter was lax, and the rectum filled with scybala and a foul watery fluid. A blood count showed Hb, 6.3 g.%; red cells, 2,060,000 per c.mm.; P.C.V., 24%; M.C.V., 116 cubic microns; M.C.H.C., 26%; white cells, 11,700 per c.mm. The serum showed no sign of haemolysis. The red cells were normal in size and shape, and were slightly deficient in haemoglobin.

The sulphaemoglobin absorption band was seen in a 1 in 80 dilution of blood. The marrow was normoblastic and active. The W.R. was negative. The urine showed albumin, R.B.C., and red-cell casts; no excessive urobilin.

Penicillin injections were given and the ulcers dressed with eusol. On March 14 a bottle of packed red cells was given. Vitamin therapy was begun and an olive-oil enema and nightly liquid paraffin were ordered. The facial oedema steadily diminished. She refused further blood transfusion and resisted all attempts at venepuncture; at times she refused other therapeutic measures such as enemata, and was morose and difficult throughout her stay in hospital. On March 25 sulphaemoglobin was detected in 1 in 50; most of the decrease was attributable to dilution by the transfused blood. It was detected in 1 in 40 on April 6, 1 in 10 on April 29, and not at all on May 19.

The anaemia improved rapidly with oral iron therapy, and the ulcers healed. On April 22 the patient was allowed up. She had no spontaneous bowel movements during her rest in bed, and frequent enemata were given. The patient went home on June 5.

Case 5

A coal-miner aged 42 was referred by his doctor because of cyanosis. He had had rheumatoid arthritis for six years, but had been working regularly for the past five years despite some pain. Every fortnight for five years his doctor had prescribed 100 powders for him, containing aspirin, phenacetin, and codeine. He admitted that he took them "more as a habit than anything." For two weeks he had been taking three askit powders a day, unknown to his doctor.

He had cyanosis, with no dyspnoea even when he ran, and no cardiac or gross respiratory disease. Rheumatoid changes involved both hands, both feet, and the right elbow. Chest *x*-ray examination showed no abnormality, and the E.S.R. was 55 mm. in one hour (Westergren). The blood contained sulphaemoglobin.

He was sent home and instructed to avoid all tablets unless prescribed by his doctor, who was asked to avoid prescribing phenacetin.

Discussion

Acetanilide and phenacetin have often been followed by sulphaemoglobinaemia (Morgan and Anderson, 1940; Lazarus, 1945; Brandenburg and Smith, 1951), and constipation has appeared to facilitate the formation of the pigment in many cases. Finch (1948) postulated that an oxidizing drug and either constipation or a sulphur-containing medication were necessary for the production of sulphaemoglobinaemia. In the present series four patients had taken phenacetin, and two of these were constipated, and the fifth patient had been taking magnesium sulphate for constipation. *In vitro*, sulphaemoglobin is easily produced by the addition to laked blood of hydrogen sulphide and *para*-aminophenol, a possible breakdown product of phenacetin in the body (Campbell and Morgan, 1939). *In vivo*, *para*-aminophenol or a related compound may act upon red cells along with hydrogen sulphide absorbed from the bowel. Such absorption would be increased by intestinal stasis, and one might suggest that the sulphide content of the bowel is increased by sulphate medicaments, since *Bact. coli* is known to reduce sulphate to sulphide.

Brandenburg and Smith (1951) noted that a large percentage of their 62 patients with sulphaemoglobinaemia were neurotic. In the present small series neurotic tendencies were observed in all four patients who took analgesics.

The analgesic of choice with the four patients was the askit powder, which, incidentally, is manufactured locally. Its appeal is twofold: 0.55 g. (8.25 gr.) of aspirin and 0.4 g. (6 gr.) of phenacetin endow it with potent analgesic properties, and 0.11 g. (1.7 gr.) of caffeine citrate provides significant cerebral stimulation, even without the other 0.1–0.2 g. of caffeine in a cup of tea. (The corresponding quantities in the *B.P.C.* tablet are 4½ gr. (0.29 g.) of aspirin, 3½ gr. (0.23 g.) of phenacetin, and ½ gr. (32 mg.) of caffeine.) The attraction of askit to the neurotic patient is undoubtedly the stimulant effect, mild though it is. Of the 62 cases of sulphaemoglobinaemia described by Brandenburg and Smith (1951), at least 44 were due to analgesic preparations containing caffeine, and Morgan and Anderson (1940) recorded a case of habituation to a tablet containing acetanilide, phenazone, and caffeine. They also pointed out that true addiction implies physical dependence on a drug, and this has not been demonstrated in the case of antipyretics or caffeine; nor did any of the present patients develop any symptoms which could be attributed to withdrawal. Their dependence had been purely psychic, and habituation is the more correct term than addiction. However, the same type of personality is liable to become a true addict, and this danger must be recognized before one prescribes alternative treatment.

Anaemia is not a usual accompaniment of sulphaemoglobinaemia, but four of the present patients were anaemic. The cause of the hypochromic anaemia in Cases 1 and 3 was not clearly established; Case 2 had a bleeding duodenal ulcer, and Case 4 a chronic superficial infection and haemo-

dilution due to water retention caused by salicylates. In none of the cases was there any evidence of haemolysis.

Treatment followed the usual lines: the offending drug was withheld and aspirin alone was given to relieve any slight pain; constipation was relieved by enemata and liquid paraffin; severe purgatives were avoided lest hyperaemia of the intestinal mucosa facilitate absorption of hydrogen sulphide and perpetuate the sulphaemoglobinaemia. Blood transfusion was required for Case 4 because of anoxia, and appeared almost life-saving. No specific treatment is of any avail. Treatment of the concomitant diseases was not altered by the presence of sulphaemoglobin, and no sequelae attributable to sulphaemoglobin were noticed.

Summary

Five cases of sulphaemoglobinaemia are described. One case followed the administration of magnesium sulphate as an aperient and the other four cases were due to analgesic preparations containing phenacetin. The presence of caffeine in such preparations is thought to induce habituation, particularly in neurotic personalities. Anaemia was present in four of the cases, but was not attributable to sulphaemoglobinaemia. The principles of treatment are enumerated.

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RISE OF SEDIMENTATION RATE AT LOW LABORATORY TEMPERATURE

ITS VALUE AS A LIVER-FUNCTION TEST

BY

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Most authors believe that a high laboratory temperature increases and a low one decreases the erythrocytic sedimentation rate (E.S.R.). Temperature, however, has been shown to exert an inconstant effect on the E.S.R., and in many cases a higher fall is recorded at a lower temperature when the test is performed simultaneously in hot and cold atmospheres (Weingarten, 1946; Buttaro and Tosti, 1946). It was also observed by Weingarten that a greater fall at lower temperature occurred in those cases which had some hepatic damage. Gupta (1954) proved that the higher fall at a lower temperature is due to a qualitative change in the euglobulin fraction of the plasma proteins. Since most of the flocculation reactions that test the liver function depend on the euglobulin fraction of the plasma proteins (Dyke, 1947), it was thought worth while to investigate if such a simple observation could be used to determine the liver damage.

Material and Method

Cases having definite liver damage were selected for investigation. These included cases of cirrhosis and cancer of the liver, infective and amoebic hepatitis, and chronic malaria and kala-azar. Most of the malaria patients had an enlarged liver, and all had an enlarged spleen and fever for more than three months.

Blood was collected in the morning, the patient having been kept fasting overnight. The E.S.R. was carried out by the Westergren method at temperatures of 99 and 44° F. (37.2 and 6.7° C.) in an incubator and a refrigerator respectively. The readings were taken every ten minutes for a period of one hour. If the E.S.R. was found more than 10% higher at 44° F. (6.7° C.) it was adjusted to be a higher fall in the cold—that is, a positive reaction for liver damage—while a greater fall at 99° F. (37.2° C.) was regarded as a negative reaction; and if the difference between the two readings was less than 10% the reaction was regarded as indeterminate.

After having observed a fairly large number of cases a comparative study was made with a number of well-established liver-function tests as controls. The control reactions were the Takata–Ara, thymol turbidity, hippuric acid synthesis, blood proteins, and the Weltmann. The tests were performed in 17 cases of cirrhosis, 10 cases each of infective and amoebic hepatitis, 12 cases of chronic malaria, and 4 cases of cancer of the liver.

The Takata–Ara, thymol turbidity, and intravenous hippuric acid tests were performed according to the technique described by Dyke (1947), and the Weltmann test as described by Tyagi (1947). Proteins were estimated in the beginning of our series by the biuret reaction (Harrison, 1947), but later on the "lumetron" photoelectric colorimeter was substituted.

Observation and Results

The results of the cases studied by the fractional estimation of the E.S.R. in the hot and cold chambers are given in Table I and those of the comparative study in Table II.

TABLE I.—*Results of E.S.R. in Hot and Cold Temperatures*

	No. of Cases	Positive	Negative
Cirrhosis	71	51 (72%)	20
Infective hepatitis	12	0	12
Cancer of liver	10	7 (70%)	2
Amoebic hepatitis	14	9 (64%)	5
Kala-azar	2	2 (100%)	0
Chronic malaria	19	15 (79%)	4

TABLE II.—*Percentage of Positives with Various Tests*

	No. of Cases	Thymol Turbidity	Takata–Ara	Weltmann Reaction	Hippuric Acid	Blood Protein	E.S.R. Hot and Cold
Cirrhosis	17	76%	82%	76%	88%	71%	76%
Infective hepatitis	10	90%	70%	50%	0%	50%	0%
Cancer liver	4	25%	100%	100%	50%	75%	75%
Amoebic hepatitis	10	50%	50%	50%	50%	25%	60%
Chronic malaria	12	66%	75%	83%	58%	75%	58%

It will be seen that 51 out of 71 (72%) cases of cirrhosis of the liver gave a positive result. Cases which showed a negative reaction were usually of long standing, some of five years' duration; and it could be concluded that in many of them the activity of the disease had come to an end. In 10 out of 20 cases which showed a negative reaction, the E.S.R. at the end of one hour was less than 20 mm., while the remainder showed a tendency towards a declining E.S.R., indicating that the activity of the lesion was waning. The positive results with other tests varied between 70 and 84%. It is of interest to quote the observations of Ernst and Dotti (1948), who while doing the thymol turbidity test on 33 cirrhotics found positive results in 22 (67%). They concluded that the compensated cirrhotics in whom there is considerable fibrosis with abdominal ascites, but in whom the remaining liver parenchyma is functioning adequately for bodily needs, do not show a rise of thymol turbidity. When, however, the remaining cells are damaged by an infection, or by a toxin, or by anoxia, then the thymol reaction becomes positive. The only three cases of alcoholic cirrhosis met with in our series gave completely negative results. It is interesting to note that Kunkel (1948) also got similar findings with the thymol turbidity and the cephalin-cholesterol flocculation tests, and in a large percentage of cases a negative reaction was consistently obtained with the two tests.

In amoebic hepatitis and abscess a high percentage of positives was obtained. Out of five cases which showed a negative

reaction four had a well-formed abscess, and the E.S.R. in the fifth was only 10 mm. It may be possible that as abscess formation took place the localization of the disease allowed other liver cells to recover and to function normally. Other tests gave positive results in about 50% of the cases. In the hands of Gminder (1939) the Takata–Ara test gave 71.4% positive, while the serum colloidal test gave completely negative results (Maclagan, 1944). In four cases of amoebic hepatitis Wahi (1946) found 100% positive results with the hippuric acid excretion test.

A negative reaction in the presence of definite carcinoma of the liver remains unexplained. In the present series 2 cases out of 10 showed a negative reaction, and in a third it was indeterminate. Ernst and Dotti (1948) also observed that in several cases of carcinoma of the stomach with extensive metastasis in the liver the thymol turbidity was not raised. He also found that primary carcinoma of the liver very often gave negative results. The thymol turbidity and colloidal gold tests gave positive results in 40% (Ernst and Dotti, 1948) and 12.5% (Cates, 1941) cases respectively.

The cases of infective hepatitis showed a general slowing of the E.S.R. This is in accord with the reports of Miles (1945) and Boveri *et al.* (1947). The one-hour reading never exceeded 20 mm. in any of them. Sedimentation in the cold chamber was, however, still lower in all; so that all the patients gave a negative reaction. The general slowing of the E.S.R. was assumed to be due to the presence of bile salts. Damodaran (1948) found that in infective hepatitis concentration of the bile salts in the blood may reach 1 in 500. According to our investigations with the same concentration of bile salts *in vitro*, the E.S.R. came to a standstill. The presence of bile salts therefore considerably handicapped the evaluation of the effect of temperature on the E.S.R. Positive results from 66% (Watson *et al.*, 1945) to 99% (Wahi, 1946) have been reported with the thymol turbidity test. Serum colloidal gives 93% positives (Maclagan, 1944), while the Takata–Ara test gives 84% positives (Wahi, 1946).

From time to time workers have reported dysfunction of liver in malaria. As reported by Carter and Maclagan (1946), the thymol turbidity test gave positive results in 80% of the cases and serum colloidal gold in 94% of them. The E.S.R. was positive in 79% of the cases of malaria and in 100% of the cases of kala-azar.

Discussion

It is seen that the percentage of positives with individual tests differs in different diseases. Tests like hippuric acid synthesis, and plasma proteins, depend on the actively functioning liver tissue, and would be positive only if a sufficient amount of the liver tissue was destroyed. Other tests which appear to depend on the quantitative and qualitative variations of globulin fraction would give a negative reaction so long as the abnormal fraction is absent or present in only small amounts.

The common flocculation tests depend on the euglobulin fraction of the plasma proteins (Dyke, 1947). A closer link between the Takata–Ara test and the higher fall of E.S.R. in the cold chamber becomes evident from the observations of Baur (1948). He observed that in many cases of parenchymal disease of the liver verified at necropsy the Takata–Ara reaction was occasionally negative when done at room temperature, but became positive when done in a refrigerator. Furthermore, in cases of hepatic damage the cold Takata–Ara reaction becomes positive sooner and remains so longer than if the test is done at room temperature.

The flocculation in the Takata–Ara test is originated by mercuric chloride and sodium carbonate, and this flocculation is enhanced when exposed to refrigerator temperature, an observation very much akin to the present one, in which rouleaux formation is influenced favourably by low temperature.

It could be said that a higher fall of the E.S.R. at low laboratory temperature will in the large majority of cases indicate liver damage. The uniformly negative results in infective hepatitis, however, cannot be adequately explained, and this is a drawback of the procedure. The general slowing of the E.S.R. in these cases was proved to depend on bile salts, yet all the cases showed a higher fall in the hot atmosphere—that is, a negative reaction.

The basis of the test is the euglobulin fraction of the plasma proteins (Gupta, 1955). The decrease of albumin and fibrinogen and the rise of euglobulin appear to be characteristic of failing liver function. It would be supposed that the diseased liver cells would not be capable of producing a special protein fraction in more than the normal quantities, and it is justifiable to assume that the euglobulin arises from extrahepatic sources, possibly the reticulo-endothelial system.

Summary

The general consensus of opinion is that the sedimentation rate of red cells increases with the increase of laboratory temperature, and vice versa. In a particular group of cases the E.S.R. is higher in a cold than in a warm temperature and (1) the accelerated E.S.R. in the cold is indicative of parenchymal liver damage; (2) the results are comparable with those obtained with other flocculation tests in general use except that the cases of infective hepatitis gave uniformly negative results; and (3) the reaction is an elaboration of a test already in universal clinical use and can be easily performed without any additional equipment: it also does not require any experience with more complicated methods, which remain the preserve of the clinical pathologist.

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The Institute of Psychiatry of the University of London, located at Maudsley Hospital, is the only university school in Britain devoted wholly to postgraduate education in psychiatry. The report from mid-1953 to mid-1954 states that the number of postgraduate students, including registrars, who received training during the year was 230, not including case workers who have spent varying periods in one or other of the departments. Students from abroad came from 25 countries. Rather more than two years ago the Guy's-Maudsley neurosurgical research unit was opened, and this has extended the clinical facilities of the Institute for teaching and research, and a number of collaborative investigations are in progress. The wider experience of temporal lobectomy for the relief of epilepsy has provided much more material than has been available hitherto, and studies to elucidate the relationship between the site of epileptic foci, the site and nature of associated lesions, the seizures, and the psychological changes have been started. In the teaching carried on at the Institute, although systematic instruction has to be given, particularly to those preparing for the D.P.M., the emphasis is on free discussion, related to reading and clinical experience.

LOW BACK PAIN TREATED BY MANIPULATION

A CONTROLLED SERIES

BY

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The patient suffering from low back pain provides one of the commonest problems encountered by the general practitioner. Working hours lost through this form of disability must add up to a vast total. The possible causes of backache are legion, and accurate diagnosis may be difficult. In 1951 the Mayo Clinic reported a series of 2,000 cases in which the cause of chronic back pain was investigated, and in 20% no definite diagnosis was reached.

Patients complaining of acute low back pain, however, form a definite clinical group. The onset is often related to strain or trauma. The lesion in such cases must be in the region of the intervertebral joints and adjacent structures. Various controversial opinions are held concerning the exact nature of these lesions and are expressed in such terminology as fibrositis, muscle strain, sacro-iliac strain, slipped disk, etc.

Manipulation as a method of treatment for such cases has been recommended by a few clinicians but condemned by the majority, although it is regularly practised, with apparent satisfaction to the patients, by the medically unqualified manipulator. To the best of our knowledge, no attempt has been made to compile a controlled series to settle the dispute. In this preliminary report we have not entered the controversy on diagnosis; we have simply sought to establish whether or not manipulation has a place in the treatment of recent low backache. Certain established concepts of the causation of low back pain are, however, worthy of mention, as their consideration has led to the form of this investigation.

The normal spine, with its series of interlocking bony units and intervertebral disks, is a resilient structure. The adoption of the upright posture and resultant curvatures provide areas where stress and strain are maximal. Boyle (1954) showed that spondylosis in the dorsal and lumbar spine most commonly affected the joints between the seventh and eighth dorsal and the third and fifth lumbar intervertebral bodies. Degenerative disk changes are common in these areas and begin early in life, leading to fibrosis, desiccation, fissuring, and possible protrusion of the cartilaginous or pulpy portions of the disk. Cyriax (1945) has postulated that minor protrusions bulging the posterior longitudinal ligament, not severe enough to cause nerve-root pressure and sciatica, can cause pain; and that this latter is due to pressure on the adjacent dura mater. Though derangement of the intervertebral joints is undoubtedly responsible for much acute lumbar pain, it is obvious that the pendulum has swung too far and diagnosis of a "disk lesion" is apt to be made too readily. Tears of adjacent muscles and ligaments may occur, or avulsion fractures of transverse and spinous processes. Spondylolisthesis, the presence of transitional vertebrae, and other minor congenital abnormalities may predispose to stress and strain injuries of the lower lumbar spine by altering local mechanics. Willis (1929) found the fifth lumbar vertebra partially sacralized in 4.7% and completely sacralized in 1.5% of 1,500 skeletons. Partial lumbarization of the first sacral vertebra in 1.2% and complete lumbarization in 4.1% of the same series were discovered.

Crisp (1952) stressed the possibility of injury to apophysial joints and nipping of synovial fringes as a cause of acute lumbar pain which is amenable to dramatic relief by manipulation.

Whenever manipulation is considered one must always be aware of the rarer and more serious causes of low back pain. These must be excluded by careful clinical and radiological examination. Such causes include osteomyelitis, tuberculous caries, ankylosing spondylitis; fractures, vertebral collapse, and other sequelae of trauma, osteoporosis, or neoplasm; Paget's disease, intraspinal lesions, and pain referred from pelvic structures. These conditions are, of course, absolute contraindications to treatment by manipulation.

Method

It was decided to divide into two groups, without selection, all patients presenting with recent low back pain. One group was treated by manipulation of the lumbar spine, without anaesthesia, according to the methods described by Cyriax (1950). The other group was treated by bed rest, the use of a lumbar pillow, and analgesics. All patients were advised on the posture to be maintained while standing and sitting, and told to avoid spinal flexion and especially bending and lifting. It was of course essential that there should be no contraindication to manipulation in any of these cases, as determined by full clinical and radiological investigation. Any patient complaining of pain radiating below the buttock, or with neurological signs such as diminished reflexes in the lower limbs, muscle weakness, or paraesthesiae, was rejected for the purpose of the present investigation. A detailed history, based on a carefully considered plan, was taken in every case and a full clinical examination made by one of us. The lumbar spine and pelvis were *x*-rayed in all cases. The information was transferred to a series of punch cards, facilitating the future assessment of each case. Each patient was seen at weekly or shorter intervals for assessment of signs and symptoms indicating improvement or deterioration. The basic features noted in the history and examination were as follows.

(1) Sex. (2) Age group. (3) Number of previous attacks of pain. (4) Site of pain, whether bilateral or unilateral. (5) Radiation of pain. (6) Whether aggravated by coughing or sneezing. (7) Whether pain is experienced on rising from bed. (8) Whether cramps are present. (9) Whether a soft or sagging bed is used. (10) Whether employment is significant (strain). (11) Whether there is a history of associated trauma. (12) Whether improving spontaneously. (13) Whether any leg shortening (½ in. (1.3 cm.) or more). (14) Lumbar lordosis. (15) Lumbar kyphosis. (16) Scoliosis—adolescent; scoliosis—relevant. (17) Other deformities. (18) Hip-joints. (19) Back flexion restricted. (20) Back extension restricted. (21) Back lateral flexion restricted. (22) Back rotation restricted. (23) Straight-leg raising restricted. (24) Any abnormality of knee-jerks, ankle-jerks, or plantar reflexes. (25) Any muscle weakness in lower limbs. (26) Any loss of sensation in lower limbs. (27) Any sign of sacro-iliac joint disease. (28) Radiological evidence of congenital abnormalities, disk degeneration, or bony disease of any kind. (29) Type of treatment employed. (30) Time in weeks after treatment started before patient is free of signs and symptoms.

As previously stated, the patients in this series were placed alternately on either manipulative treatment or rest in bed and analgesics. Some of them did not carry out instructions or did not report for assessment, and have been discarded from the final series. Thus the original two groups, each of 76 patients (152 patients in all), are unequal in the final figures (76 and 60).

Results

The results of the investigation are given in tabular form. The patients treated by manipulation are referred to as Group I and those treated by rest and sedation as Group II. Age and sex distribution are shown in Table I. It was remarkable that the proportion of males was the same in each group, being 62%.

TABLE I.—*Age and Sex Distribution*

Age	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0–19	2	3	1	2	1	4	2	3	1	3	1	4
20–29	19	25	10	21	9	31	8	13	3	8	5	22
30–59	50	66	33	70	17	58	45	75	29	78	16	69
60+	5	7	3	6	2	7	5	8	4	11	1	4

Table II shows the number of previous attacks of acute lumbar pain in both groups.

TABLE II.—*Previous Attacks*

No.	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1 ..	22	29	15	32	7	24	17	28	11	30	6	26
2 or 3	4	5	3	6	1	3	9	15	6	16	3	13
More than 3	22	29	15	32	7	24	12	20	5	13	7	30
None	28	37	14	30	14	48	22	37	15	40	7	30

Information regarding the site of pain is given in Table III.

TABLE III.—*Site of Pain*

	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Central lumbar	54	71	33	70	21	72	42	70	30	81	12	52
Unilateral ,, ...	33	43	21	44	12	41	20	33	12	32	8	35
Bilateral ,, ...	13	17	5	11	8	28	11	18	8	22	3	13
Radiation pain	28	37	17	36	11	38	24	40	15	41	9	39

Other information obtained from the history of the patients is shown in Table IV.

TABLE IV

	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Aggravated by coughing	46	60	30	64	16	55	41	68	25	68	16	69
Sagging bed used ..	14	16	9	19	5	17	17	28	12	32	5	22
Employment significant	25	33	22	47	3	10	20	33	19	51	1	4
Associated history of trauma	39	51	25	53	14	48	27	45	19	51	8	35
Improvement occurring	26	34	16	34	10	34	22	37	14	38	8	35

Information obtained from clinical examination is given in Table V.

TABLE V

	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Restricted lumbar flexion	48	63	32	68	16	55	33	55	22	60	11	48
,, ,, extension	27	36	17	36	10	34	26	43	17	46	9	39
Restricted lateral flexion	31	41	18	38	13	45	27	45	18	49	9	39
,, rotation ..	16	21	10	21	6	21	11	18	8	22	3	13
Straight-leg raising diminished	39	51	27	57	12	41	26	43	21	57	5	22
X-ray films:												
Congenital abnormalities	9	12	7	15	2	7	9	15	8	22	1	4
Radiological evidence of disk lesion ..	8	11	3	6	5	17	10	17	6	16	4	17
*Other lesions ..	17	22	12	25	5	17	21	35	11	30	10	43

* Osteophytosis, osteoarthritic changes, etc.

The results of treatment are given in Table VI.

TABLE VI

	Group I (76)						Group II (60)					
	Total		M 47		F 29		Total		M 37		F 23	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Well in 1 week	38	50	24	51	14	48	16	27	11	30	5	22
With Lasègue's sign initially	20	26	15	32	5	17	10	17	8	22	2	9
Well in 3 weeks ..	28	37	18	38	10	34	20	33	13	35	7	30
,, ,, 6 ,, ..	1	1	0		1	3·5	7	12	5	13	2	9
Persistent symptoms and signs after 6 weeks	9	12	5	11	4	14	17	28	8	22	9	39
With Lasègue's sign initially	3	4	2	4	1	3	6	10	3	8	3	13
With congenital abnormalities	1	1·3	1	2	0		2	3	2	5	0	
With radiation of pain initially	3	4	1	2	2	7	7	12	3	8	4	17

Discussion of Results

From the information obtained, we have selected certain groups of figures which we regard as of significant value. Statistical analysis has not yet been applied, because the present preliminary figures are inadequate for this purpose.

The distribution of male to female patients was 3:2. Most patients were in the age group 30–59 years and had suffered no previous attack or only one previous attack of pain. About 70% of each group complained of central lumbar pain. Unilateral and bilateral lumbar pain were much less common (see Tables I, II, and III).

There was no obvious percentage difference between male and female patients except in the group of "significant employment." As one might expect, there was a great predominance of males. Aggravation of pain by coughing occurred in about 65% of each group and each sex. The use of a sagging type of mattress, often a feather bed, may be an important factor, being noted in about 20% of all cases. Trauma might be expected to play an important part, and about 50% of the patients in each group gave such a history, with disability coming on within a short period of time (see Table IV).

The commonest signs found on examination were painful restriction of lumbar spinal flexion, occurring in about 60% of each group, and diminished straight-leg raising predominantly on one side, which occurred in about 50% of each group (see Table V).

There was a higher percentage of congenital abnormalities present than in the general population, by comparison with Willis's findings, especially of sacralization or lumbarization of L 5–S 1 vertebrae. This suggests that such malformations make the back mechanically unsound and prone to lesions causing backache in later life (see Table V).

Of the patients manipulated 50% were free of signs and symptoms at the end of one week as compared with 27% in the control group (see Table VI). At the end of six weeks only 12% of Group I were suffering from signs and symptoms, while 28% of Group II were still affected.

Perusal of that Table as a whole shows how simple manipulation of the lumbar spine, in the type of case described, results in freedom from symptoms and disability more quickly than does rest. It should be remembered, moreover, that the spinal manipulations were carried out by both physiotherapy students and trained staff, and the figures thus include many cases treated by relatively unskilled therapists.

It may be noted that of the patients in each group who were well after one week, over half had diminished straight-leg raising originally. If a Lasègue sign is taken to indicate a disk lesion, albeit of slight degree, then manipulation had helped to relieve it.

Of the patients in each group who still had signs and symptoms after six weeks, only a small proportion had Lasègue's sign originally on examination. It may also be noted that few of these patients had congenital abnormalities.

A relatively high number of this resistant group had radiation of pain initially, and this may be an important symptom in predicting response to treatment in either group.

Conclusion

In the patient with acute low back pain in whom the probable lesion is derangement of an intervertebral joint, including minor protrusion of a disk, and in whom irritation or pressure on adjacent structures occurs, then treatment by manipulation, without anaesthesia, seems a logical method of gaining relief from signs and symptoms.

Summary

A group of 152 patients suffering from acute low back pain were selected at random and treated either by manipulation or by bed rest and analgesics.

Full clinical and radiological examination was carried out in every case, and progress, whether improvement or deterioration, was noted at weekly intervals.

Of the patients manipulated, 50% were symptom-free and discharged within one week and 87% were discharged within three weeks.

Of the patients treated by rest in bed and analgesics, 27% were symptom-free and discharged within one week and 60% within three weeks.

After six weeks, 12% of the patients treated by manipulation, and 28% of the patients treated by rest in bed and analgesics still suffered pain and disability.

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Medical Memoranda

Amyotrophy Due to Hypoglycaemia

Neurological disturbances often occur in hypoglycaemia. Transient asphasia and hemiplegia are not uncommonly seen in hypoglycaemia due to insulin overdosage. More profound disturbances may occur, particularly in cases of islet cell tumour, when considerable diagnostic difficulty may be encountered. Lawrence *et al.* (1942) have described in detail the changes in the brain in six fatal cases of hypoglycaemia. There was widespread degeneration and necrosis of the nerve cells, particularly in the cortex, putamen, and caudate nucleus, with slighter changes in the brain-stem and cerebellum. The changes are probably due to failure of the normal cellular oxidative processes from glucose lack, although vascular factors may play a part. Rarely, lesions of the lower motor neurone, probably on the same pathological basis, may occur. Moersch and Kernohan (1938) mention loss of the anterior horn cells from a segment of the lumbar cord in an account of the changes in the nervous system from a fatal case of hypoglycaemia. Tom and Richardson (1951) describe a case of islet-cell adenoma, undiagnosed in life, which showed severe muscle atrophy of the legs. Histological examination of the spinal cord from this case showed destruction of the anterior horn cells. Roxburgh (1954) mentions wasting of the small hand muscles in the report of an islet-cell tumour in a child of 5½ years. Other cases have been described by Lidz *et al.* (1949) and Silfverskiöld (1946). The latter described two cases under the title of "polyneuritis hypoglycemica." There is no record concerning the degree, if any, of recovery, but in the case recorded by Lidz the mental state and ataxia improved after removal of an islet-cell adenoma, but the muscle-wasting remained unaltered.

Case Report

The patient was a married man aged 28 years. His past medical history was uneventful and there was no family history of nervous disease. He worked as a fitter in a large factory, but was not exposed to danger of poisoning by heavy metals or organic compounds. For at least twelve months prior to admission to hospital he complained of feeling weak, tremulous, and "queer" after any undue exertion. This often happened at his work, particularly just before lunch, after which he felt quite well again. There were times when he was unable to concentrate on his work, and his memory became rather capricious. During a holiday in June, 1953, he was found unconscious one morning and admitted to the local hospital. On examination he was found to be conscious but aphasic and there were signs of a right hemiparesis. The blood sugar concentration was 30 mg. per 100 ml., and he recovered fully and promptly following an intravenous injection of 20 ml. of 50% glucose. As he was on holiday he was given a high-fat, high-protein, low-carbohydrate diet and told to report to his doctor on his return home. His doctor referred him to Walton Hospital on August 13, 1953. He was then feeling better and refused in-patient investigation. He remained well until January, 1954, when his symptoms recurred. His wife stated that it became very difficult to wake him in the mornings until he was given a sweet drink. He had short episodes of mental confusion terminating in an attack of sweating, and was amnesic for these episodes. Both he and his wife realized that taking sugar prevented these symptoms, and he eventually carried sugar with him.

He was admitted for investigation on February 8, 1954, with the provisional diagnosis of spontaneous hypoglycaemia. He was tall and spare of build; his colour was good; and examination of the chest, heart (blood pressure 130/70 mm. Hg), and abdomen showed no abnormality. He gave the impression of being a little slow mentally. The pupils reacted normally and no abnormality was seen in the fundi; ocular movements were full, but there was nystagmus on extreme lateral gaze in both directions. There were no cranial-nerve palsies. The musculature of both shoulders and upper arms appeared to be a little wasted, but there was no detectable weakness. Both hands showed marked wasting of the intrinsic muscles, the interossei and hypothenar groups in particular. There was a little weakness of the extensors of the fingers. The tendon reflexes in the arms were brisk and equal and there was no subjective or objective sensory loss. Co-ordination was normal. The abdominal reflexes were present and equal. There was symmetrical wasting of both quadriceps, with marked fasciculation and fibrillation. The glutei and hamstrings were powerful, but there was some weakness of dorsiflexion of the left foot with a little associated wasting of the anterior tibial muscle group. The knee- and ankle-jerks were brisk and equal, and the plantar responses flexor. There was no objective sensory loss, and tests of co-ordination were normal.

Three successive fasting tests resulted in hypoglycaemia after periods of approximately twelve hours: blood-sugar values were 40, 40, and 35 mg. per 100 ml., and administration of intravenous glucose resulted in prompt recovery on each occasion, thus fulfilling Whipple's criteria. A glucose-tolerance test following a diet containing 350 g. of glucose for three days gave the following figures: fasting, 85 mg.; half an hour after 50 g. glucose, 100 mg.; 1 hour after, 85 mg.; 1½ hours after, 70 mg.; 2 hours after, 50 mg. per 100 ml. The haemoglobin was 93% and the white cell count 11,000 per c.mm., the differential count being normal. Liver function tests, including serum bilirubin, thymol turbidity, and serum alkaline phosphatase, were normal. *X*-ray films of the chest, skull, and cervical spine showed no abnormality. Lumbar puncture revealed clear fluid under

normal pressure, with one cell per c.mm. and a protein content of 32 mg. per 100 ml. The blood Wassermann reaction was negative. The electroencephalogram showed rather excessive low amplitude, slow activity.

At operation (Mr. N. O. K. Gibbon) on February 28 a single plum-coloured growth the size of a pea was found in the head of the pancreas and removed without undue difficulty. Convalescence was uneventful. Post-operative hyperglycaemia was not observed, the fasting blood-sugar values falling between 95 and 114 mg. per 100 ml. A glucose-tolerance test done ten days after operation gave the following results: fasting, 95 mg.; half an hour after 50 g. glucose, 130 mg.; 1 hour after, 120 mg.; 1½ hours after, 100 mg.; 2 hours after, 100 mg. per 100 ml.

Section of the tumour revealed an insulinoma, which was thought to be benign. The patient was discharged, symptomless, on March 20. When seen in the out-patient department six weeks later he felt very fit. He was working regularly and was symptom-free. The nystagmus had disappeared, but the muscle-wasting was unchanged.

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Foster Kennedy Syndrome Produced by Myelomatous Deposits in the Skull

The complete Foster Kennedy syndrome comprises an association of anosmia, primary optic atrophy and central scotoma, and contralateral papilloedema. The essential features of the syndrome are the atrophy and papilloedema, either or both of the other two components often being absent. The syndrome was first described in detail by Foster Kennedy (1911). It is usually produced by olfactory groove or sphenoidal meningiomas or by frontal-lobe tumours (Walsh, 1947). Its occurrence in any other condition is a rarity, and it is accordingly commonly seen in the 40–60 age group. Clearly, the syndrome may be due to any space-occupying lesion near to the olfactory tract.

The case described below is exceptional in that the compression was due to myelomatous deposits. Multiple myeloma also occurs most frequently after the age of 40 (Snapper, 1949). In this case the patient was unusually young, and the manner in which the case presented was more suggestive of a cerebral tumour than of myelomatosis.

CASE REPORT

A male steel worker aged 34 was first seen on July 30, 1953, complaining of generalized aches and pains which he had had for six months. These had at first affected his back and pelvic region. Later his shoulders and neck were involved. After these pains had been present for four to five weeks he developed severe frontal headaches. All these symptoms, with the exception of the headache, disappeared spontaneously five to six weeks prior to admission to hospital.

For five to six weeks before admission he had noticed that his left eye was beginning to protrude. There was no associated deterioration of vision. At the same time he developed intractable vomiting, which occurred 10 to 15 times a day. He also complained of general weakness, loss of weight, and recent nocturnal frequency of micturition. On inquiry he admitted that his food had recently become tasteless.

On examination he was clinically anaemic, but otherwise appeared in fair general health. There was marked proptosis and epiphora of his left eye. The patient had no sense of smell. There was neither diplopia nor ophthalmoplegia. The left fundus showed primary optic atrophy with an occasional blotchy haemorrhage near the disk. In the right fundus the whole disk was ill-defined, the veins were prominent, and the complete lack of contour and blurring of the edge of the disk indicated a moderate degree of papilloedema. In addition several blotchy haemorrhages were present, mostly near the disk. The visual fields were normal, but the visual acuity of the left eye was diminished to 6/9, while that of the right eye was 6/6. He was tender over the fifth and sixth ribs on the left side. No further abnormalities were found.

Several laboratory investigations were carried out. The urine contained Bence Jones protein, but showed no other abnormality. The blood urea was 155 mg. per 100 ml. and his urea clearance was 15% of average normal standard clearance. The findings in the serum were: alkaline phosphatase, 13 K.A. units; acid phosphatase, 3 Gutman units; total protein 8.8 g. per 100 ml. (albumin 5.7 g., globulin 3.1 g.); sodium, 135 mEq/l.; potassium, 6.5 mEq/l.; alkali reserve, 18 mEq/l.; chloride, 88 mEq/l.; calcium, 12 mg. per 100 ml. The peripheral blood examination showed: haemoglobin, 51% (7.5 g. per 100 ml.); red cells, 2,500,000 per c.mm.; C.I., 1; leucocytes, 6,000 per c.mm. (neutrophils 3,000, eosinophils 60, lymphocytes 2,340, monocytes 600); no plasmacytes were seen; platelets, 250,000 per c.mm. (Lempert); E.S.R. (Westergren), 124 mm. in one hour.

Marrow smears from the right and left iliac crests and from a radiologically evident myelomatous deposit in the left clavicle showed gross infiltration with cells of the plasmacytic series, consistent with a diagnosis of myelomatosis.

Pentamidine isethionate was given by intramuscular injection on alternate days to a total of 4 g. over a period of six weeks. The patient also received deep *x*-ray therapy, 2,500 r depth dose to the anterior fossa of the skull, between August 12 and 28.

After these measures the proptosis and papilloedema disappeared, whilst the vomiting gradually ceased. It was at first thought that the vomiting may have been due to chronic renal failure, but as the blood urea level did not fall concurrently with the decline in vomiting it was concluded that the latter was caused by the raised intracranial tension.

COMMENT

This case presents several unusual and interesting features. Multiple myelomatosis in a man of 34 is rare. The youngest in Bayrd and Heck's (1947) series of 83 cases was 37. Though myeloma deposits are often found in the skull, producing the characteristic radiological appearance, it is relatively rare to find the tumour extending beyond the confines of these bones. This was observed in only two cases in the series quoted above. Accordingly, only exceptionally is intracranial tension raised in myelomatosis. Snapper (1949) states: "Although myeloma so often involves the skull, no convulsive seizures have been observed and the optic disks never show evidence of increased intracranial pressure." In the present case there were definite signs of raised intracranial tension—namely, papilloedema, retinal haemorrhages, and vomiting. Lumbar puncture was thought to be inadvisable in these circumstances, and so no direct measurement of the C.S.F. pressure was made. The only component of the Foster Kennedy syndrome that was lacking was the central scotoma.

I wish to thank Professor E. J. Wayne for permission to publish this case; Dr. E. K. Blackburn for the interpretation of the marrow smears and other haematological data; and Dr. G. M. Wilson for his help and encouragement.

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Reviews

ACTIVE TRANSPORT AND SECRETION

Active Transport and Secretion. No. VIII, Symposia of the Society for Experimental Biology. (Pp. 516+vi; illustrated. 45s.) Cambridge University Press. 1954.

The transfer of substances and ions across membranes and diffusion barriers in general is a most important subject of study by experimental biologists at the present time. Much is now known about the intracellular enzymes which are concerned with intermediary metabolism, but how a substrate reaches its specific enzyme system within the cell is still obscure. The existence in the cell of structures which possess their own membranes—for example, mitochondria—shows that the selection of the desirable substrate from among the diversity of substances presenting at the cell surface is only one of many problems to be considered.

This volume contains the papers read at a symposium of the Society for Experimental Biology held in July, 1953, and includes contributions emanating from departments of agriculture, botany, zoology, physiology, biochemistry, biophysics, pharmacology, clinical pathology, and experimental medicine. The subject-matter of the papers is as diverse as their origins, but some unification is achieved in a final article by J. F. Danielli entitled "Morphological and Molecular Aspects of Active Transport." Professor Danielli discusses six morphological levels at which it is profitable to consider active transport: (1) the simplest known cellular membranes such as those of red blood cells; (2) cell membranes which are specialized for the performance of active transport, such as those of intestinal epithelial cells, kidney tubule cells, and motor end-plates; (3) mitochondria; (4) vacuoles; (5) pinocytosis—the absorption of environmental fluid as discrete droplets by undulating membranes; and (6) extracellular processes, such as the flow of lymph and pumping activity of intestinal villi. Each morphological unit can display different processes of transport—for example, simple diffusion, facilitated diffusion, and active transport. Simple diffusion is the movement of molecules in an unrestricted manner under the driving force of thermal agitation; facilitated diffusion occurs also under the driving force of thermal agitation, but is restricted both by structural and by steric factors and has been recognized as occurring only at "active patches" in the cell surface; in active transport molecules, etc., are transferred across barriers by the use of an energy supply other than, or in addition to, that of thermal agitation. The energy supply needed for active transport will clearly be derived from metabolic processes, and so the study of enzymes and the effects of enzyme poisons in relation to the processes of active transfer is a rapidly developing one. Various molecular models for the intimate mechanism of active transfer have been postulated, of which that of a propelled shuttle moving forwards and backwards across the membrane, and that of a molecular carrier rotating within the membrane, are the most fashionable. The idea that, in relation to active transport, enzymes may possess important mechanical as well as catalytic functions is an interesting one that needs much further investigation. All these matters will be of significance to those, among many others, who are interested, for instance, in the processes of kidney secretion and absorption, in the mechanisms involved in nerve condition, in the absorption of fat from the intestine, and in the transference of passive immunity from mother to foetus.

This volume, apart from one isolated instance, contains no record of the discussion that took place at the symposium; but, since the book in its present form contains over 500 pages, the inclusion of the discussions would have made it somewhat unwieldy. A more serious omission is that of an index, in the absence of which the book loses much of its potential value for reference to the present views of active investigators in a field that is necessarily somewhat diffuse. Nevertheless this volume, which represents a valuable conspectus of expert opinion on a subject of wide importance, can be read with profit by all those to whom the mechanisms of transport and secretion are of interest.

F. G. YOUNG.

LEUKAEMIA RESEARCH

Ciba Foundation Symposium on Leukaemia Research. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Margaret P. Cameron, M.A., A.B.L.S. Assisted by Joan Etherington. (Pp. 297+xiv; 56 illustrations. 30s.) London: J. and A. Churchill Ltd. 1954.

The symposium of which this is a transcript was arranged in order to take stock of the present position of research in leukaemia. There is suggestive evidence that leukaemia is increasing, and that this is a true increase and not merely an improvement in diagnosis. The disease is inevitably fatal, and research is therefore attended by a certain sense of urgency. Among the main topics discussed was, first, the relevance of animal research in leukaemia to the human disease. Though most of our knowledge of leukaemia has come from observations in man—as, for example, the therapeutic value of arsenic, *x* rays, nitrogen mustard, and the folic-acid antagonists—and though the transmitted strains of leukaemia used by experimentalists differ in many ways from the spontaneous disease, we shall probably be increasingly indebted to animal research for new remedies against leukaemia and related maladies. A second main topic was the role of a virus in the aetiology of leukaemia, and particularly the interesting results obtained by L. Gross in the transmission of leukaemia to the newborn mouse. A third topic was the induction of leukaemia by ionizing radiations and the protection obtained by shielding the spleen or injecting emulsions of spleen, bone marrow, or other cells.

The symposium was an exciting one to attend, and this monograph will be a stimulus to existing and would-be researchers in this field. It will join the list of key books on leukaemia, which already includes Claude Forkner's *Leukaemia and Allied Disorders in Man,* unhappily not revised since its publication in 1938, and Engelbreth-Holm's *Spontaneous and Experimental Leukaemia in Animals,* published in 1942.

L. J. WITTS.

THE TRIAL OF CRAIG AND BENTLEY

Trial of Christopher Craig and Derek William Bentley. Edited by H. Montgomery Hyde, M.P. (Pp. 264; illustrated. 15s.) London, Edinburgh, and Glasgow: William Hodge and Co. Ltd. 1954.

On November 2, 1952, Craig and Bentley were observed breaking into a warehouse; the police were informed, and subsequently Craig shot and killed P.C. Miles when the latter, with other policemen, was attempting to apprehend him. Bentley had already been arrested. Craig, the leading spirit, could not by law be hanged, as he was under 17 years of age. He was apparently an aggressive, callous, illiterate youth, being unable to read, owing, it is claimed, to word-blindness. The reasons for the indignation aroused by the hanging of Bentley (aged 19) were pithily expressed in Parliament by Mr. R. T. Paget, Q.C., M.P.: "A three-quarters witted boy is to be hung for a murder he did not commit and which was committed 15 minutes after he was arrested." In his address to the jury the Lord Chief Justice explained the law concerning the common responsibility of accomplices in crime in the following terms: "When two people are engaged on a felonious enterprise—and warehouse-breaking is a felony—and one knows that the other is carrying a weapon and there is agreement to use such violence as may be necessary to avoid arrest and this leads to the killing of a person, both are guilty of murder." Interesting legal problems were: How long does common responsibility endure? What are the criteria for its termination? Might not the fact of arrest be considered to terminate it? And, if not necessarily so, in what conditions would it not be so?

It would seem that Bentley made legal history by being the first to be hanged as an accomplice in a crime for which the principal in the first degree could not be executed on the grounds of age. Moreover, Bentley was considerably below average in intelligence, and it was said, according to the editor of this book, that he had been reported as mentally deficient at an approved school and had been rejected on mental grounds for National Service. Like Craig, he was illiterate.

This trial doubtless possesses considerable legal interest; from the medical point of view the interesting thing is that the medical aspects—the apparently low mentality of the two boys, and particularly of Bentley—were not raised in their defence. The introduction is clear; but Mr. Montgomery Hyde might have spared us his views on the causes of juvenile crime and such *obiter dicta* as that "it is a sad reflection on our times that both these youths were found at their trial to be practically illiterate."

DESMOND CURRAN.

SOCIAL MEDICINE

The Meaning of Social Medicine. By Iago Galdston, M.D. (Pp. 137+viii. 22s.) Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1954.

Beatrice Lillie used to include in her wartime repertory a soprano launched on a song which she and her audience soon recognized was beyond her resources. As she approached the top note it became clear to all concerned that she wasn't going to make it, so she hastily dropped an octave and tried to pass it off as though nothing had happened. This essentially is the procedure followed by Dr. Galdston in his discussion of the meaning of social medicine. He provides an interesting account of the development of modern medicine, which he suggests has failed because it has been concerned with the treatment of disease rather than with the promotion of health. As a result, lowered mortality rates have not been accompanied by a commensurate improvement in health and well-being. Social medicine, apparently, is to put this right. But at the point at which we should expect to be told how this is to be done the subject is dropped, and the book ends on a different note, with two chapters on "Social Medicine and Medical Education" and "Social Medicine in Great Britain." It is not the first time that recognition of a problem has been mistaken for its solution.

It is hard to see why people still find it necessary to make exaggerated claims for a new subject. One would have thought it quite sufficient if in, say, ten years the decision to establish departments of social medicine seemed in retrospect to be a right one. But the late Professor René Sand regarded social medicine as "the final flowering of the preventive and curative arts," and Dr. Galston conceives it as "the corrective and fulfilment of the modern biological sciences." These are claims which would tax the combined resources of the Royal Colleges and the Royal Society. Fortunately we can accept less; we shall certainly have to.

THOMAS MCKEOWN.

"BALANCED" ANAESTHESIA

The Practice of Balanced Anesthesia. By Sylvan M. Shane, D.D.S. Preface by Juan White Morquecho, M.D. (Pp. 196; illustrated. $5.75.) Baltimore: Lowry and Volz. 1953.

In case the reader is uncertain about the meaning of "balanced anaesthesia" a definition is supplied in the preface written by Professor Juan White Morquecho, of Mexico City, who says that balanced anaesthesia "consists of a series of proceedings in which the pharmacodynamic qualities of different therapeutic agents are taken advantage of in a rational manner." This definition clearly covers practically the whole of clinical anaesthesia. Indeed, though the author says that his book is "not a treatise on anaesthesia," it is just that—though not a very good one. The central theme is the use of a "balanced mixture" consisting of oxygen, nitrous oxide, and cyclopropane in certain proportions; but the author does not hesitate to add morphine, barbiturates, and other drugs before, and barbiturates, relaxants, and analgesics during, the operation. The full range of spinal and local analgesia is also employed.

The dust cover says that the book was written for the physician, dentist, nurse, and veterinarian. In this country, at all events, only the last three might find the book of use. Postgraduates will find the standard far below the level they must aim at, while the general practitioner will almost certainly not extend his practice to this extent. The list of references given is inadequate for any serious purpose. The book hardly represents a worthwhile addition to the medical literature on anaesthesia.

W. W. MUSHIN.

A GREAT HOSPITAL

The Brompton Hospital: The Story of a Great Adventure. By Maurice Davidson, M.A., D.M., F.R.C.P., and F. G. Rouvray, O.B.E. (Pp. 152+viii; illustrated. 21s.) London: Lloyd-Luke (Medical Books) Ltd. 1954.

A hundred years ago patients suffering from consumption were not admissible to the voluntary general hospitals in London. It was owing to the enterprise and energy of Philip Rose, and to a lesser degree of John Labouchere, that the Brompton Hospital for Consumption and Other Diseases of the Chest was opened in 1842. At first the out-patient department was in Great Marlborough Street, and the in-patients were accommodated in the Manor House, Chelsea. In 1854 the north wing of the present structure was opened. We were interested to learn that in the early days the applicants for the post of assistant physician to the hospital were submitted to a clinical test of their competency before they were considered eligible for the post. In 1871 Miss Cordelia Angelica Read left £100,000 to the hospital, which enabled the south wing to be built and opened in 1882. The will containing the legacy was found in the locked drawer of a spinet, which (we are glad to know) is still preserved in the hall of the hospital.

In this beautifully produced book Dr. Davidson and Mr. Rouvray graphically describe the development of this world-famous hospital, and give pen-pictures of many of the distinguished physicians who helped to build up its reputation. They also point out how the rapid growth of surgery of the chest has improved the treatment and prognosis of many conditions. They rightly emphasize the importance of the hospital in undergraduate and postgraduate teaching. "L'Envoi," with which the book ends, is a beautiful and moving termination of a noteworthy record of a great hospital.

ZACHARY COPE.

The distinguished French medical historian Charles-Victor Daremberg, who died in 1872, left unfinished a comprehensive bibliography of medicine. This was completed by Alphonse Pauly and published in 1874. It was intended to include all important works published to that date, including all titles found in Haller, Choulant, and Callisen, arranged chronologically under each subject. This *Bibliographie des Sciences Médicales*, out of print for many years, has now been reproduced in facsimile and published by Derek Verschoyle, 13, Park Place, London, W.1, for £8 8s. Its appeal will be chiefly to collectors and bibliographers.

There have been no major changes in either the arrangement or the content of the *Hospitals Year Book 1954–55*, although a minor addition is of a list of British Standards relating to hospital equipment. There is, however, an editorial article of some importance on the best use of hospital resources, which gives a report on the progress made in hospital services since 1948 and outlines the main weaknesses and problems which require consideration if the service is to be run efficiently and economically. The *Year Book*, which costs £2 2s., can be obtained from the Institute of Hospital Administrators, 75, Portland Place, London, W.1.

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THE DISCOVERY OF PENICILLIN

The discovery of penicillin introduced a new epoch in the treatment of disease. It has been followed by an intense search for other "antibiotics," and a whole range of bacterial infections have now come within the effective control of substances produced, for the most part, by moulds, among which *Penicillium notatum* holds pride of place not only historically but also therapeutically. We stand so close to a bewilderingly rapid sequence of discoveries that as yet we probably fail to understand fully the revolution in medicine that has taken and is taking place as a result of Alexander Fleming's discovery. It is natural that the world will acclaim a medical advance "great" in proportion to the curative benefits it brings, and on this count alone Sir Alexander Fleming has his place among the immortals. And close beside him will be Sir Howard Florey and Dr. Ernst Chain, who in a systematic investigation of antibacterial substances ten years later hit upon the technical ways and means of fulfilling the promise Fleming held out for penicillin in 1929. Fleming had the real naturalist's capacity for observation and the scientific imagination to see the implications of the observed fact—a capacity and an imagination which, it is true, only the prepared mind can compass, and which in the great discovery seem invariably to be joined to a mind that is essentially humble. As there have been some popular misconceptions of the part Fleming played in discovering penicillin it may not be inappropriate at this time of his death to recall in his own words some of the observations he summarized in his historical paper in the *British Journal of Experimental Pathology* for June, 1929:

"A certain type of penicillium produces in culture a powerful antibacterial substance."

"The active agent is readily filterable and the name 'penicillin' has been given to filtrates of broth cultures of the mould."

"The action is very marked on the pyogenic cocci and the diphtheria group of bacilli."

"Penicillin is non-toxic to animals in enormous doses and is not irritant. It does not interfere with leucocytic function to a greater degree than does ordinary broth."

"It is suggested that it may be an efficient antiseptic for application to, or injection into, areas infected with penicillin-sensitive microbes."

The discovery recorded in Fleming's paper is a milestone in the history of medical progress, and the "penicillin" he discovered and named has come nearer than any other remedy to Ehrlich's ideal therapia sterilisans magna.

ANTICHOLINERGIC DRUGS FOR PEPTIC ULCER

During the past few years a spate of anticholinergic drugs have been introduced for the treatment of gastro-intestinal disorders, particularly peptic ulcer and enterospasm. Belladonna has had a time-honoured role, and these new preparations have sought to emulate its action but with fewer undesirable side-effects. "Banthine" (methantheline bromide) blazed the trail and has been followed by a bewildering number of other drugs, including "antrenyl," "bentyl," "centrine," "lergine," "lytensium," "merbentyl," "monodral," "pamine," "prantal," and "wyovin," and much has been written on both sides of the Atlantic about their pharmacological and clinical effects. In the *Journal* this week a special study of lergine (tricyclamol chloride) is presented by Drs. Pamela Aylett and A. H. Douthwaite.

All these drugs have much in common. Their chemistry is complex; they achieve an anticholinergic effect like atropine by blocking transmission either at autonomic ganglia or at the peripheral effector site; they reduce basal secretion, slow the emptying time of the stomach, and lessen intestinal muscular activity. Although side-effects are generally claimed to be slight, in practice the usual atropine-like disturbances of impaired vision and dryness of the mouth are quite common, and sometimes there may be constipation and difficulty in urination. Moreover, the response varies considerably between different patients and even in the same patient at different times.

The therapeutic contribution of these new drugs is not impressive, and they have not greatly advanced the therapy of peptic ulcer. Nor were they likely to do so, since atropine and related drugs, although undoubtedly beneficial for smooth-muscle spasm, have never been conclusively proved to give great benefit in cases of peptic ulcer, though most clinicians would agree that belladonna can help to relieve pain, particularly night pain, in duodenal ulcer. According to Nicol[1] even large doses of atropine had very

[1] Nicol, B. M., *Lancet*, 1939, **2**, 881.
[2] Rowlands, E. N., *et al.*, ibid., 1952, **2**, 1154.
[3] Friedlander, P. H., ibid., 1954, **1**, 386.
[4] Texter, E. C., and Barborka, C. J., *Postgrad. Med.*, 1954, **16**, 449.

little effect on the acid of the stomach when measured over 24 hours, and no better success seems to have been achieved by ganglion-blocking agents in this respect.[2] It has been postulated that slowing the stomach's rate of emptying would allow the more effective use of antacids, but this hypothesis is by no means proved. The distension of the stomach is itself an important stimulus to secretion, and slowing of the rate of emptying may well mean more prolonged secretion, which would offset the neutralization. However, using tricyclamol, Drs. Aylett and Douthwaite have prolonged the period of achlorhydria from 1¼ to 2½ hours after a dose of aluminium hydroxide, but details of only two patients are given. Again, the inhibition of other intestinal secretions, particularly pancreatic, might offset any benefit to the duodenum from lowering of the gastric acidity. Indeed, in so far as these drugs are supposed to help the healing of peptic ulcer, the administration of them is still based on doubtful hypotheses and insufficient clinical study with control series.

The clinical evidence of the value of methantheline in controlled observations is unimpressive apart from some reduction of pain, and P. H. Friedlander[3] did not find that the natural history of duodenal ulcer was improved. E. C. Texter and C. J. Barborka[4] followed 250 patients with proved peptic ulcer for two years. The patients were treated identically with diet and the usually recommended forms of treatment, the only difference being that half the patients received 100 mg. of methantheline four times a day, while the remainder received 0.4 mg. of atropine sulphate four times a day. After the two years these authors, without knowledge of which drug had been given, then assessed the patients' progress: they found that those taking banthine were symptomatically improved and had had somewhat fewer and milder recurrences than those taking atropine. The recurrence rates were high in both groups—75% in the banthine group and 90% in the atropine group. When the results were separated into mild, moderate, and serious cases, the best results occurred in the group whose ulcers had been classified as mild before treatment, whereas in the group with severe ulcers it mattered little whether atropine or banthine had been used. Complications and the need for surgery were of the same frequency in the two groups. Therefore the conclusion was that, although these drugs often gave symptomatic improvement, the eventual course of the disease was not altered.

But, while the natural history of the disease is not materially influenced, greater relief of pain is important to the patient and justifies the administration of any of these preparations during the phase of active ulceration, though it would seem reasonable to see whether the desired effect cannot be obtained with the traditional belladonna before prescribing the new, and much more expensive, preparations. The *tab. belladonnae et phenobarb.* of the *National Formulary* contains ¾ gr. (50 mg.) of phenobarbitone and ⅔ gr. (26 mg.) of the dry extract of belladonna and is convenient to prescribe when some sedation is required as well.

It may be unfashionable to say so, but patients appreciate brand-new treatments, and it is an advantage to have a variety of compounds available for the management of a chronic and relapsing disease. Apart from some difference in side-effects, it is unlikely that any one of the many new preparations will prove to be superior to its rivals, and the family doctor need not feel that he must personally evaluate each preparation.

EXCHANGE TRANSFUSION

No effective prophylaxis is yet available against maternal iso-immunization from rhesus and other blood-group incompatibility between mother and foetus. The problem of preventing stillbirths from this cause is still unsolved, in spite of attempts to reduce the effects of foetal haemolytic anaemia by cortisone administration to the mother[1–3] or inducing labour early in a few selected cases.[4] Treatment has therefore been concentrated on the 70% of affected babies who are born alive. The main complications in untreated infants are anaemia at birth in about two-thirds, which may be progressive, and kernicterus after 36 hours in up to a quarter. Adequate exchange blood transfusion with fresh compatible packed cells not only corrects severe anaemia without increasing blood volume but also reduces the risk of kernicterus by removing up to 1,000 mg. of bilirubin contained in over 85% of the infant's sensitized red blood cells. In our opening pages Drs. W. Walker and G. A. Neligan, of Newcastle, report the results of 250 exchange transfusions, with a remarkably low mortality of only 15 deaths attributable to haemolytic disease of the newborn. A follow-up of 200 of the survivors showed only 3 suffering from kernicterus, confirming the good long-term prognosis found by P. Armitage and P. L. Mollison.[5] They also discuss the modern indications for the procedure

[1] Hunter, O. B., Jr., *J. Amer. med. Ass.*, 1954, **154**, 905.
[2] Wiener, A. S., ibid., **155**, 63.
[3] DeCosta, E. J., *et al.*, *Obstet. Gynec.*, 1954, **3**, 131.
[4] Davies, B. S., *et al.*, *Arch. Dis. Childh.*, 1953, **28**, 466.
[5] Armitage, P., and Mollison, P. L., *J. Obstet. Gynaec. Brit. Emp.*, 1953, **60**, 605.
[6] Wiener, A. S., *et al.*, *J. Pediat.*, 1954, **45**, 546.
[7] Diamond, L. K., *Pediatrics*, 1948, **2**, 520.
[8] Mollison, P. L., and Cutbush, M., *Advances in Paediatrics*, Chapt. 5, 1954, London.

and the increasingly important technical details of it, and underline the advantages of exchange over simple transfusion. A. S. Wiener *et al.*[6] have also emphasized this recently and reported a reduction in mortality (including kernicterus survivors) from 46.4% to 15.5% in comparable severe groups.

The greatest benefit is obtained from exchange transfusion when it is carried out within a few hours of birth with not less than 60 ml. of packed cells per lb. (170 ml. per kg.) on affected infants who are anaemic, premature, or are considered likely to develop kernicterus. Treatment is probably ineffectual once neurological signs of kernicterus have appeared, so prediction is essential. Consequently treatment may be said to begin with routine antenatal care, parental blood grouping, and maternal antibody determinations during pregnancy. These measures enable the arrival of most of the affected infants to be predicted, and hospital delivery can be arranged: birth is followed by the rapid performance of the direct Coombs test and rhesus blood-group test on the baby's cord blood. Treatment is then planned in accordance with haemoglobin levels in the cord blood. If necessary bilirubin determinations and normoblasts and reticulocyte counts can be done. The mortality of full-time babies delivered in hospital in Walker and Neligan's series was only a quarter that of babies admitted after birth, a cogent argument in favour of hospital delivery when maternal sensitization is discovered. About 60% of all serologically affected babies receive exchange transfusion. They include all babies with positive direct Coombs tests, with the exception of full-time infants with a cord haemoglobin level above 15 g. per 100 ml. Above 17.5 g. per 100 ml. there appears to be no danger of kernicterus, but the borderline group with cord haemoglobin between 15 g. and 17.5 g. per 100 ml. appear to run a 10% risk of kernicterus if untreated. However, if all in this group have exchange transfusions, the percentage of babies receiving replacements would rise considerably and many would be subjected unnecessarily to a procedure which carries a definite mortality, though small in skilled hands. The policy in the past has been to practise expectant treatment in this borderline group, unless jaundice develops rapidly after birth or an affected infant has been born to these parents previously. Here, Walker and Neligan make another important contribution, for they found that a cord bilirubin level of less than 2.8 mg. per 100 ml. carried no risk of kernicterus in the borderline group, in which it occurred in four-fifths. Thus routine testing of bilirubin levels in cord blood may help in the prognosis of difficult cases. Exchange transfusion cannot entirely prevent kernicterus, but among over 200 Newcastle babies receiving exchange transfusion were only 5 cases of kernicterus in spite of limiting a second exchange transfusion to 4 babies. The authors recommend re-exchange if the bilirubin level rises above 25 mg. per 100 ml. after the first transfusion. Other authorities have re-exchanged up to 20% of babies, including also those who are premature or who have a history of a previously affected sibling. The kernicterus rate in Diamond's[7] series of 257 affected babies, 87% of whom received exchange transfusion once and 20% twice, was 2%, and total mortality 13%. Mollison, however, points out that a second exchange transfusion is only one-seventh as effective in removing the infant's bilirubin.[8] The effect of modern treatment can be gauged by the results in 125 receiving exchange transfusion out of 217 affected babies born in hospital in Newcastle in 1952 and 1953; the mortality was as low as 3.5%, including those due to anaemia and kernicterus, a figure which would be difficult to surpass even with wider indications for repeated exchange transfusion. It is a tribute to the skill and efficiency of a trained team.

The indication for late simple transfusion after replacement is usually a haemoglobin less than 8.5 g. per 100 ml. in the first six weeks of life, during which serial haemoglobin determinations should be made even after adequate exchange transfusion. The use of fresh donor blood within three days minimizes the dangers of transfusion reaction or hyperkalaemia due to leakage of potassium from the donor red cells into the plasma. Neligan and Walker met no complications from infection, air embolism, or portal thrombosis, but they emphasize the dangers of perforation of the umbilical vein. The umbilical route is convenient, for it usually requires no separate incision and may be patent for several days. The venous pressure can be measured before beginning exchange transfusion, and the danger of overloading the circulation in anaemic babies can be avoided by preliminary withdrawal of 10–50 ml. of blood. Because of the danger of circulatory failure, great care should be exercised if this deficit is made up later in the transfusion. Exchange transfusion should also be borne in mind in the treatment of premature infants, some of whom develop hyperbilirubinaemia and kernicterus in the first ten days of life in the absence of any blood-group incompatibility. The only prophylaxis would appear to be exchange transfusion, which many centres for the care of premature babies are beginning to carry out as soon as deep jaundice appears. Thus, exchange transfusion may continue to be carried out on newborn babies even if a method of preventing blood-group incompatibility is discovered.

REGIONAL COLITIS

As B. N. Brooke[1] points out in the opening paragraph of his recent monograph, there was, for a long time, a tendency to diagnose as ulcerative colitis almost any case of chronic diarrhoea for which there was no obvious cause. Closer study of the clinical features and of the pathology of such cases (and for this the increasing interest of surgeons in their management has been largely responsible) has now made it possible to group together certain patients in whom the disease seems to follow a distinctive pattern. Although granular proctitis or procto-sigmoiditis may be regarded by some[2] as a mild, but occasionally progressive, form of ulcerative colitis, there are several clinical features typical of this group of which spurious diarrhoea, with real constipation, and rectal bleeding seem to be the most constant. Much less frequently the surgeon sees patients in whom shallow ulceration of the mucous lining of the small intestine seems to be the primary lesion, the colon being attacked only by its later extension distally. They constitute a second and smaller (and a more controversial) group best known as ileo- or entero-colitis.[3 4] Disordered small-bowel function and anaemia are prominent symptoms, and, in general, surgery has little to offer in their relief; it is, in fact, best avoided.[3] Apart from the remaining majority of cases with the familiar diffuse ulceration affecting predominantly the distal part of the colon—and ending so often in total colectomy—is yet another distinctive group—namely, regional (or segmental) colitis.

Although the early reports of this form of ulcerative colitis (the term being used in its widest sense) date from the days of Moynihan,[5] Mayo Robson,[6] and Dalziel,[7] its wide recognition belongs to more recent times, when Crohn and his colleagues[8] first described a granulomatous lesion affecting the ileum. This is the commonest site of the disease, which on this side of the Atlantic is so often associated with his name. It has since been clearly established that segments of the large gut may be similarly affected. Since both the prognosis and the treatment differ considerably from those of ulcerative colitis, it is important that the condition should be clearly recognized, and therefore two recent reports from the Mayo Clinic,[9 10] one clinical and one pathological, are specially welcome.

It used to be the practice to refer to this form of segmental colitis as "right-sided colitis,"[11] but the term seems to be no longer suitable, for in this series the left side of the colon was affected almost as often as the right. The segments of affected bowel seem to the naked eye to be sharply marked off from the adjoining healthy gut, and even microscopically the disease seldom spreads further than a distance of 6 cm. As in the small gut, skip areas are sometimes found, as is direct extension to the rectum and to the ileum (one in four cases). The bowel is reddened, contracted, thickened, and inelastic; there is a noticeable increase in the subserous fat and fibrous tissue as well as great thickening of the submucosa, with stricture as an occasional complication. Although ulceration of the mucous membrane is one of the prominent features, and although polypoid hyperplasia may result, the threat of cancer seems to be less urgent than in true ulcerative colitis.

It is a disease of rather young people, the maximum incidence falling between 20 and 30. The onset may be so acute that the patient may come to immediate laparotomy as an abdominal emergency.[12 13] More often it is insidious, and the urgency of the symptoms thereafter varies considerably. Diarrhoea is by far the most common symptom, accompanied usually by griping abdominal pain and by obvious rectal bleeding in about half the cases. Physical examination is often quite unhelpful apart from evidence of weight loss and anaemia. Of the complications, perirectal and perianal suppuration is the most frequent. In a group of 201 patients[9] rather more than one in ten when first seen already showed evidence of infection in this situation and eight had already undergone operations on this account before the underlying disease was recognized. Medical treatment by rest in bed, dieting, and the cautious use of antibiotics was tried in 150 cases, but two out of three later relapsed. Although the group surgically treated was only a third as large, the recurrence rate was appreciably lower. Experience seemed also to show that a short-circuiting procedure has a higher record of success than a resection, whether immediate or staged. In any event, there seems to be very good reason in such cases not to overlook the diagnosis, and every justification to expect a cure by some surgical manœuvre short of an ileostomy and colectomy.

[1] *Ulcerative Colitis and its Surgical Treatment*, 1954, Edinburgh, Livingstone.
[2] Goligher, J. C., *Lancet*, 1953, **2**, 38.
[3] Brooke, B. N., and Cooke, W. T., *Lancet*, 1951, **2**, 462.
[4] —— ibid., 1953, **1**, 1220.
[5] *Edinb. med. J.*, 1907, **21**, 228.
[6] *British Medical Journal*, 1908, **1**, 425.
[7] Ibid., 1913, **2**, 1068.
[8] *J. Amer. med. Ass.*, 1932, **99**, 1323.
[9] Neuman, H. W., *et al.*, *Surg. Gynec. Obstet.*, 1954, **99**, 563.
[10] —— and Dockerty, M.B., ibid., 1954, **99**, 572.
[11] Crohn, B. B., and Berg, A. A., *J. Amer. med. Ass.*, 1938, **110**, 32.
[12] Brownlee, T. J., *Brit. J. Surg.*, 1951, **38**, 507.
[13] Thompson, H. R., *Proc. roy. Soc. Med.*, 1950, **43**, 685.

SULPHAEMOGLOBINAEMIA

Chronic cyanosis unaccompanied by signs of cardiac or respiratory disease or by polycythaemia may be due to the presence of sulphaemoglobin or methaemoglobin in the blood. Methaemoglobin results from the oxidation of haem, while sulphaemoglobin is thought to be due to the entry of sulphur into the pyrrole component of haemoglobin. The methaemoglobin disappears rapidly, but sulphaemoglobin persists as an inert compound in the erythrocyte until the cell is destroyed, and is therefore more commonly encountered in clinical practice. Both pigments can be identified spectroscopically by the presence of characteristic bands in the red part of the light spectrum. The patient, in spite of a striking leaden cyanosis, suffers no ill effects, apart from the theoretical disadvantage of a decrease in the blood's capacity for carrying oxygen. Sulphaemoglobinaemia is almost invariably caused by drugs, the most important of which are the coal tar derivatives, acetanilide and phenacetin, the earlier sulphonamides,[1] and nitrogen-containing compounds such as nitrites and nitroglycerin.

[1] Archer, H. E., and Discombe, G., *Lancet*, 1937, **2**, 432.
[2] Harrop, G. A., and Waterfield, R. L., *J. Amer. med. Ass.*, 1930, **95**, 647.
[3] Brandenburg, R. O., and Smith, H. L., *Amer. Heart J.*, 1951, **42**, 582.

It is difficult to estimate the incidence of the condition from reports in the literature, but it is probably uncommon.

Dr. T. B. Begg reports five patients with sulphaemoglobinaemia on p. 701 of the *Journal* this week, and points out certain interesting features. Four were taking a proprietary compound containing phenacetin, and the fifth used magnesium sulphate to treat her constipation. G. A. Harrop and R. L. Waterfield[2] induced sulphaemoglobinaemia in dogs by aniline derivatives and sulphur, and it seems likely that cyanosis results from the combined action on the red cells of an oxidizing agent and hydrogen sulphide. *Bacterium coli* in the gut is known to reduce sulphates to sulphides, and three patients in the present series suffered from constipation; this is probably more than a coincidence,[3] and would presumably facilitate absorption of sulphides. Women are more commonly affected than men, and neurotic traits are often present. Begg suggests that the patient becomes habituated to the stimulant effect of the caffeine in tablets containing aspirin, phenacetin, and caffeine, originally taken for their analgesic properties. Treatment is obvious: removal of the offending drug and its substitution if necessary by aspirin, relief of constipation without purging, and the correction of anaemia if present. A low-residue diet which is free from sulphur-containing foods, especially eggs, is sometimes prescribed. The cyanosis will persist for at least two months because of the life span of the red cells. No way is yet known of increasing the elimination of sulphaemoglobin.

OPHTHALMIA NEONATORUM

For purposes of notification ophthalmia neonatorum denotes conjunctivitis occurring in the newborn infant and includes almost everything from frank gonococcal ophthalmia to slight crusting of the lids. At the end of the last century gonococcal ophthalmia of the newborn was a common cause of blindness and its prevention a major public health problem. It was Credé's[4] introduction of cleansing the eyes of newborn infants and instilling silver nitrate drops that did much to alter this state of affairs. But social changes and the efficient treatment of gonococcal infection have combined to make maternal gonorrhoea a rarity in most hospitals, and this has led to a revaluation of the use of prophylactic drops. In a recent paper from Australia Ida Mann[5] finds that silver nitrate has some effect in preventing "sticky" eyes, though she considers that it is responsible for provoking a sterile discharge in the first day or two of life in some babies. In general her findings agree with the earlier work of Taylor and Calman[6] at Queen Charlotte's Maternity Hospital, and like them she feels that the use of silver nitrate is unnecessary in a modern hospital. Furthermore, in an institution where adequate bacteriological examination of all infected eyes is a routine, the very rare case of gonococcal ophthalmia is diagnosed so early and treated so readily as to present no cause for anxiety.

Other forms of prophylaxis have been suggested from time to time. The instillation of a single drop of penicillin solution appears to have no rational basis, but the use of an ointment containing 100,000 units per gramme of penicillin, originally suggested by Davidson and his colleagues[7] from the Johns Hopkins Hospital, appears to have more to recommend it. There are two distinct objectives in the use of prophylactic drops. The first is its original purpose of preventing gonococcal ophthalmia, and the second is to reduce the incidence of "sticky" eyes. Most of the latter are staphylococcal in origin, and penicillin ointment would be unlikely to be of much value, since so many hospital strains of staphylococci are penicillin resistant. On the whole it seems that in hospitals serving a population in which gonorrhoea is rare the best treatment of the babies' eyes is simple cleansing, though the medical attendant on the spot may decide that local circumstances warrant other treatment. Elsewhere some form of prophylaxis should still be practised. As a prophylactic agent silver nitrate has some dangers—in particular, it can become dangerously caustic if concentrated by evaporation, and it can also decompose on exposure to light—so the use of penicillin ointment has something to recommend it. Other antibiotics can be incorporated in an ophthalmic ointment, and might well be effective in reducing "sticky" eyes in the days immediately after birth, though O'Brien[8] found terramycin ointment of only slight value for this purpose. The danger in recommending their widespread use for prophylaxis would be that the hospital strains of staphylococci might rapidly become resistant. Unfortunately, too, no amount of drops or ointment placed in a baby's eye at birth can prevent the numerous cases of staphylococcal eye infections occurring later in the puerperium.

VITAMIN A AND HYDROCEPHALUS

For several years Continental paediatricians, especially in France and Spain, have reported the transient appearance in infants of symptoms of acute intracranial hypertension following the administration of large doses of vitamin A. The French workers J. Marie, G. Sée, and R. Sauvant have recently summarized[1] this work, and they add further observations which define the disturbance more precisely. Thus, the ingestion of 350,000 international units of vitamin A results in malaise, restlessness, either insomnia or torpor, and often vomiting; occasionally the temperature rises. Within 24 hours the anterior fontanelle is obviously bulging, but no further abnormal physical signs appear; the fundi and electroencephalograms are unchanged. The cerebrospinal fluid is of normal composition, but the pressure is up to 150–230 mm. water, rising to 200–230 mm. on jugular compression. The disturbance fades after 24 hours, and after 48 hours the infant returns to normal. In parallel with this the level of vitamin A in the blood serum shows a sharp rise at 6 hours after ingestion, falling again after 12 hours. The authors have

[4] *Die Verhütung der Augenentzündung der Neugeborenen.* 1884. Berlin.
[5] *Brit. J. Ophthal.*, 1954, **38**, 734.
[6] *J. Obstet. Gynaec. Brit. Emp.*, 1948, **55**, 642.
[7] *J. Amer. med. Ass.*, 1951, **145**, 1052.
[8] *Lancet*, 1952, **1**, 347.

[1] Marie, J., *et al.*, *Sem. Hôp. Paris*, 1955, 31st year, 251.
[2] Millen, J. W., *et al.*, *Lancet*, 1953, **2**, 1234.
[3] *British Medical Journal*, 1954, **1**, 809.
[4] Millen, J. W., *et al.*, *Lancet*, 1954, **2**, 679.

also reproduced a similar disturbance in young puppies, and they find evidence that it can occur in older human subjects whose fontanelles have closed.

They argue that the intracranial hypertension is attributable to an acute hydrocephalus resulting from the excessive transient formation of cerebrospinal fluid. Here it should be noted that vitamin A does not pass the blood–brain barrier, and the alternative possibility that the disturbance is due rather to cerebral oedema is not discussed. Since it is reproducible in young animals, the possibility could readily be tested. Should it eventually be established that excess of vitamin A promotes a sharp increase in the flow of cerebrospinal fluid, it would be peculiarly difficult to reconcile such a finding with the work of Millen and his co-workers at Cambridge, who claim that internal hydrocephalus is produced in young animals by too little vitamin A. Although in their first publication on this subject,[2] which was noticed in this *Journal*,[3] they attributed the hydrocephalus to stenosis of the aqueduct, in a later publication[4] they found reason to shift their ground. Intensifying the degree of maternal hypovitaminosis, they obtained earlier stages of the disease in their newborn and foetal rabbits. In these the aqueducts were not obviously different from those of controls, and they concluded that the stenosis observed in later stages was somehow a secondary effect of the hydrocephalus. In seeking for the cause of the hydrocephalus they were driven to the conclusion that excessive formation of cerebrospinal fluid was the only feasible mechanism. We are thus faced with the unlikely proposition that either too much or too little vitamin A can promote this disorder. It remains to be seen which is correct.

PHYSIQUE AND CHARACTER

Comparing Oxford undergraduates with Chelsea pensioners, Lipscomb and Parnell[1] have found that the pensioners as young men were nearly 4 in. (10 cm.) shorter and 25 lb. (11.3 kg.) lighter than the undergraduates. At the average age of 73 the fifty pensioners' heights had not altered significantly, but they were then only 5 lb. (2.3 kg.) lighter than the undergraduates. In spite of this weight gain they still had less subcutaneous fat than undergraduates, and a greater proportion of the weight was contributed by bone and muscle. Somatotyping showed them to be mainly mesomorphs, with a few mesomorphic-ectomorphs. Those who gained most weight rated most highly in endomorphy. By means of his "clock" method[2] of simplified somatotyping,[3] based on height, weight, and three skin-fold measurements, Parnell found that over 95% of the pensioners were muscular and wiry, compared with fewer than 40% of undergraduates. The results of this investigation illustrate the value, as pointed out by Parnell in an early paper,[4] of this method of clinical examination "in the practice of medicine, the study of healthy people, care of orphans or children in approved or ordinary schools, investigation of the benefits or otherwise of games and physical training, study of fertility or populations, personal relationships within the family or in communities, nutritional requirements, in surveys of crime, delinquency, and indeed almost every study of mankind. In short there is hardly a topic of social interest from murder to matrimony on which records of constitution do not touch and cannot quicken interest." Sheldon and Stevens[5] correlated different character traits with different somatotypes. They found that among mesomorphic people "group action was the keynote, vigour of thought, vehemence of expression, aggressiveness and energetic reaction, bold directness of manner, love of exercise, adventure, chance and combat, these were the prominent features. Problems were met by action, not by submission or by acceptance." And now the bemedalled heroes of the Royal Hospital, Chelsea, who have exhibited these very character traits more convincingly perhaps than any other single group of men in the world, are found to be "mainly mesomorphs with a few mesomorphic-ectomorphs." Surely the important bearing that this might have on physical standards of recruiting cannot be missed.

MacQueen[6] has pointed out that it is possible to augment the musculature by modern techniques of progressive resistance exercise, probably well beyond the one-unit difference on the seven-point scales mentioned by Parnell.[7] Muscular bulk so achieved is maintained with little subsequent training,[8] and it is tempting to believe that by influencing the physique towards mesomorphy the character traits of this somatotype may also be developed. Rigorous physical training in the preflight schools of the American Army Air Forces tended to level the differences between endomorphic and ectomorphic aviation cadets.[9] Parnell[10] has found that mesomorphic students seek psychiatric advice least often, and endomorphic-ectomorphs have the highest prevalence of psychiatric and psychosomatic disorders. It is possible that a physical training regimen may reduce the incidence of these disorders in students and may even have some therapeutic value in psychiatric and psychosomatic medicine.

Kretschmer's original system of somatotyping has been superseded by that of Sheldon and his collaborators.[11 12] To Parnell we owe the evolution of a greatly simplified method[13] which can be quickly learned and applied in routine clinical examination. It may yet be questioned whether medical students learn enough of the variations of normal human constitution. The culture of the physique together with the culture of the mind was a prominent feature in ancient civilizations, and its present lack may be a fault in modern living.

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[1] Lipscomb, F. M., and Parnell, R. W., *J. roy. Army med. Cps*, 1954, **100**, 247.
[2] Parnell, R. W., *Eugen. Rev.*, 1952, **44**, 20.
[3] Sheldon, W. H., *et al.*, *The Varieties of Human Physique*, 1940, New York and London.
[4] Parnell, R. W., *Eugen. Rev.*, 1952, **44**, 20.
[5] Sheldon, W. H., and Stevens, S. S., *The Varieties of Temperament*, 1942, New York and London.
[6] MacQueen, I. J., *British Medical Journal*, 1954, **2**, 1193.
[7] Parnell, R. W., *Med. Press*, 1954, **231**, 3.
[8] Delorme, T. L., and Watkins, A. L., *Progressive Resistance Exercise. Technics and Medical Applications*, 1951, New York.
[9] Schneider, E. C., and Karpovich, P. V., *Physiology of Muscular Activity*, 3rd edition, 1948, Philadelphia and London.
[10] Parnell, R. W., *Modern Trends in Psychosomatic Medicine*, 1954, London.
[11] Sheldon, W. H., *et al.*, *The Varieties of Human Physique*, 1940, New York and London.
[12] —— *Atlas of Men*, 1954, New York and London.
[13] Parnell, R. W., *Amer. J. Phys. Anthrop.*, 1954, **12**, 209.

EMERGENCIES IN GENERAL PRACTICE

HAEMATEMESIS AND MELAENA

BY

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It is estimated that between 20,000 and 30,000 patients are admitted to hospital annually in England and Wales for serious gastro-duodenal bleeding. In most cases this is sudden, dramatic, and urgent, and the haemorrhage is obvious, either as a frank haematemesis or as a sudden and unmistakable tarry stool, often with diarrhoea. The vomit may be dark, like coffee-grounds, owing to the conversion of haemoglobin into acid haematin in the stomach, or it may be fresh and red just as it comes from an arterial haemorrhage. In either case it usually differs from a severe haemoptysis by being acid in reaction and non-frothy, unlike blood brought up from the lungs. The patient may be severely shocked and actually faint, or he may only become cold, weak, and restless. The pulse is quick, the blood pressure low, a cold sweat develops, and the patient, especially if elderly, often becomes confused and delirious. Pallor may be intense, and a peculiar pinched appearance of the face and nose is sometimes very striking.

In some cases, however, bleeding is insidious and difficult to recognize, so that it may continue unsuspected for long periods. It is important to remember, not only that blood oozing from the upper part of the alimentary tract may be insufficient in amount to turn the stools black, but also that patients do not in all cases take notice of dark stools, even if they are passed. In any cases of unexplained pallor, fainting, weakness, or symptoms of anaemia such as dyspnoea on exertion or oedema of the ankles the patient should be questioned about the colour of his motions and asked to notice them, particularly if he has not previously done so; it must not be forgotten, however, that many "tonics" and dyspeptic mixtures contain iron or bismuth, which darken the stools, and that much meat or green vegetables such as spinach have the same effect. A history that the patient has passed dark stools must not, therefore, at once be accepted as evidence of bleeding, and whenever possible this must be checked by a chemical test for occult blood. These tests are simple to perform, require no elaborate technique or materials, and can be carried out easily by the practitioner himself; the finding of such melaena demands, of course, a full history, examination, and investigation.

The simplest test is the Gregerson,* and for this it is not necessary to ban chlorophyll-containing foods, meat, or iron mixtures from the diet, as an immediately positive result definitely indicates blood, whilst a faintly positive one may be ignored. The possibility that the blood has come from the mouth, or from piles, or from swallowing sputum must, of course, be remembered in assessing the significance of a positive test.

**Gregerson's Test.* A powder containing 0.29 g. of barium peroxide, with 0.025 g. of benzidine, is dissolved in 5 ml. of glacial acetic acid and a few drops of the solution are run on to a thin smear of faeces on a filter paper. A blue colour appearing at once or within a few seconds indicates the presence of blood, but appearing only after 20 to 30 seconds is of no significance.

Causes of Bleeding and Differential Diagnosis

Many large series of cases of haematemesis have been published, and from these and from my own experience the main causes, with their percentage incidence in Britain, may be approximately classified as follows:

Chronic duodenal ulcer	40	70
Chronic gastric ulcer	30	
Acute ulcer (gastro-duodenal erosions)	20	
Cirrhosis of the liver	5	
Carcinoma of the stomach	3	
Other causes	2	

In practice, the distinction between a chronic duodenal ulcer and a chronic gastric ulcer may be impossible to make and is, in fact, of relatively little importance compared with the vital distinction between an acute erosion and a chronic ulcer. This is a matter of extreme importance, since in the former case any form of surgical treatment is contraindicated, whilst in the latter it may be urgent and life-saving. In some cases the diagnosis is clear, since previous radiological examination may have shown an ulcer, and the history may be typical. In others it may be highly suggestive from the characteristic periodicity and the pain–food relationship.

It is rare, but by no means unknown, for a patient who has a chronic recurrent ulcer to deny any previous indigestion, but as a rule sudden haematemesis, with no history of any preceding pain or dyspepsia, is likely to be due to an acute erosion. This cause of bleeding is not well understood. It is certainly not infrequent, and, if *all* those cases in which no exact cause can be found and barium-meal examination is negative are grouped under this heading, it probably accounts for some 20 to 30% of all gastro-duodenal haemorrhages.

In some cases there is a strong presumption that an irritant drug may have caused the haemorrhage, and it is always important to inquire whether the patient had a cold, toothache, or a headache before the bleeding, as he may very well have forgotten that he had taken aspirin, "veganin," or some similar tablet, which might have caused the erosion. Drugs in tablet form are particularly concerned, and in a few cases the patient may know that he is sensitive to aspirin. In others expectorant mixtures containing quinine or ipecacuanha, or drugs such as phenylbutazone or *para*-aminosalicylic acid, precipitate bleeding, as may some sedatives, such as "sedormid."

Bleeding from an acute gastric erosion is often very severe, and often occurs in young people in apparently perfect health, and for no apparent reason that they can give. There is no tenderness or evidence of ulcer, and no history pointing to liver disease or primary blood dyscrasia. In a few cases the haemorrhage has recurred on several occasions, as neither the patient nor his doctor has been able to discover any cause.

Recurring haematemeses, however, for which no ulcer or other lesion has been found, may have some other less frequent, but important, causes, one of which is particularly characteristic—namely, hereditary telangiectasia. In this condition, multiple angiomata occur and as a rule can be found on examination, especially on the face, lips, or mouth, and there is a family history of gastric bleeding. The patient has almost always suffered from severe epistaxis during infancy and childhood. In one patient, aged 71, there had been over a dozen severe gastric haemorrhages since the

age of 30, on almost every occasion needing transfusion, and he had been once explored and eight times submitted to *x*-ray examination for ulcer, with negative results. There had never been any pain or indigestion, but, on questioning, he admitted to dangerous bouts of nose-bleeding when he was a small boy. On examination a few naevi were found on the skin, and at a second operation, which was undertaken after a radiologist had demonstrated a supposed gastric ulcer niche after a barium meal, no sign at all of any ulcer was found and the diagnosis of hereditary telangiectasia was confirmed.

In cases of portal hypertension with cirrhosis of the liver the haematemesis is also painless, but there is often a history of dyspepsia and the patient may have been a heavy drinker or have had recurrent jaundice (hepatitis); spider naevi may be found on the skin, with sometimes a characteristic facies. The liver is often palpable and in some cases the spleen also; but absence of these findings does not by any means exclude cirrhosis. The distinction from chronic ulcer, whilst often very difficult, is an extremely important one, since morphine, anaesthetics, and operation all carry serious risks in cases of cirrhosis.

Other causes of bleeding are much less frequent but may sometimes present difficulties in diagnosis. Blood diseases, such as leukaemia or purpura, heart failure, and hypertension may occasionally lead to haematemesis, and the rather more frequent hiatus hernia, with oesophagitis or ulcer, and carcinoma of the oesophagus or stomach must also be thought of. In rare cases a gastric polyp may be a cause of recurrent severe haemorrhage without pain.

Treatment of Severe Cases

The atmosphere of panic and alarm which a severe haematemesis produces in the patient and in those around him may easily spread to the doctor, and it is vital to keep calm and to give an air of reassurance and confidence as much as possible. In actual fact it is rare in these cases for a few minutes to become a matter of life and death, and it is a good thing to stress the favourable aspects of the emergency, the high recovery rate, and the well-understood lines of treatment. It may, with advantage, be pointed out that a loss of 10 to 12 pints (6 litres) of blood is not more than the body can tolerate without very serious danger, and a pint (about half a litre) is a usual amount for a blood donor to give. The degree of haemorrhage can be roughly estimated by the pallor, coldness, sweating, and collapse of the patient, the rate of the pulse, and the level of the blood pressure.

The first essential is to keep the patient warm by blankets or hot-water bottles, but this does not mean overheating. It is indeed important not to overdo it, for though the skin temperature may be low, this is partly nature's protective means of conserving internal heat, and it is unwise to promote undue dilatation of skin vessels and increase perspiration, which of course favours dehydration. Provided, however, that fluids are allowed—as they should be—some external warmth is advisable and is certainly of much comfort to the patient.

If there is much dyspnoea oxygen should be given, but this is of relatively little value if the haemoglobin to carry the oxygen is very low, and in any case is almost useless if given by the old method of holding a funnel in front of the patient's face. Some means, such as a plastic bag, a mouthpiece fitting the patient, or a nasal catheter must be adopted, but even if this is done it is not likely to be of much help if there is only pallor without cyanosis. If the haemorrhage is severe, the home conditions are bad, the patient is alone or in a hotel, or has little help available, admission to hospital is essential. The dangers of an ambulance journey are far less than those of remaining at home—but it is usually quite safe to wait a short time before having the patient moved. During this time, if the blood pressure is very low, it is worth raising the foot of the bed, but drugs to raise the pressure, such as noradrenaline, are not advisable unless a blood transfusion can be given simultaneously to replace the blood lost. When telephoning the hospital it is helpful to give details of age, pulse rate, and blood pressure rather than the bare statement of a haematemesis. The use of morphine, ¼ gr. (16 mg.) hypodermically, to calm the patient and relieve shock is at this stage usually advisable, but the exact dose and the time it is given must be told to whoever takes the patient to hospital. The dangers of morphine in haematemesis are of causing undue depression of the medullary centres, especially in elderly patients with emphysema, or of the case proving to be one of cirrhosis of the liver, in which even the normal dosage may cause deep coma. It must not be forgotten also that in a very appreciable number of patients morphine itself causes vomiting, so that a dangerous vicious circle may be set up. These dangers do not, however, loom so large in the case of the initial dose given at the time of the bleeding, which greatly helps the patient to withstand the ambulance journey to hospital, as in subsequent doses.

During the first hour or two after a severe haemorrhage it is often advised to give the patient nothing by mouth at all, but frequent small drinks of cold water or fruit juice, 2 to 3 fl. oz. (60 to 90 ml.) at a time, are both safe and necessary and give some slight feeling of confidence also.

No medicines, other than morphine, are indicated at this stage, either orally or by injection, but later a sedative is often advisable, and then paraldehyde, 3 or 5 ml. intramuscularly, is very useful, or soluble phenobarbitone, 3 gr. (0.2 g.) subcutaneously, may be used. Alkalis have little if any place in treatment. If the patient remains in his home a nurse should be in attendance, and blood should be taken as soon as possible for grouping and estimation of the haemoglobin. More elaborate analysis of the blood chemistry—non-protein-nitrogen, sodium, chloride, and potassium—requires a skilled laboratory and hospital facilities.

Intravenous Therapy

In cases of moderate severity the question of intravenous therapy may not arise, but in more serious cases, if vomiting continues at all, an intravenous drip must be set up at once. The main indications for giving intravenous fluids are thirst, a dry tongue, oliguria, and a low blood pressure. If a drip is needed, intravenous glucose–saline should be given at the rate of about 100 drops a minute for the first one or two litres, after which the rate must be slower and accurate control of the electrolyte balance of the body becomes essential.

Blood transfusion may be a life-saving measure, but should not be given as a routine. It is the only effective and really physiological means of raising blood pressure if the patient is intensely blanched, shocked, and dyspnoeic; in this case the use of packed cells may enable a large oxygen-carrying capacity to be given in a relatively small volume. Any risk that such transfusion may provoke further bleeding is very small indeed, and if the blood is given slowly is almost negligible, whereas the continuation of a seriously low blood pressure is an urgent danger to life and far outweighs any fears of fresh bleeding resulting from the rise of pressure after transfusion.

In less urgent cases blood need not necessarily be given unless the haemoglobin is below 50% and the systolic blood pressure falls below 80. The patient's pulse should be charted hourly, and if the rate remains at about 120 a minute this generally means that bleeding is continuing, and is one of the clinical indications for blood transfusion. It must be remembered that the haemoglobin estimation immediately after haemorrhage may be deceptively high owing to the concentration of the blood which follows the bleeding, whilst later it is proportionately reduced by dilution with tissue fluids drawn into the circulation to maintain the blood volume. In elderly patients with emphysema it must also be remembered that there may have been some pre-existing polycythaemia and perhaps hypertension which may give a false impression of the haemoglobin and blood pressure.

Less Severe Cases

In many cases, however, the condition is not serious enough for any more elaborate measures to be needed than rest, warmth, and careful feeding. There need be no fear of giving some food and drink at the earliest stage. If the patient is thirsty he must be encouraged to drink in frequent small amounts, and cold milk or fruit drinks may be left at the bedside. Light solids may also be given from the beginning, though here it may be left largely to the patient's feelings whether he takes them or not. In younger patients solids, such as bread-and-butter, apple jelly, cream cheese, boiled egg, custard, junkets, or stewed fruit are usually welcomed within an hour or two of the bleeding, but with older patients it is often better to offer them only purées, malted-milk drinks, or jellies, without pressing them to take more. Chicken, fish, and lightly cooked tender meat may be given on the second or third day if the patient desires. At all costs thirst and hunger must be prevented, and even if the patient is afraid to eat or drink he should be encouraged to do so.

Operation

The later treatment depends upon the cause of the haemorrhage. If the patient is known to have a chronic ulcer, the question of emergency surgery must be considered from the start. Immediate operation, carried out with the help of blood transfusion, offers the chance of stopping the bleeding and radically treating the ulcer by partial gastrectomy at one and the same time, and is often advisable if expert surgical and hospital facilities are at hand. Such treatment is urgently called for if the patient has a second haematemesis within 24 to 48 hours of the first, if his age is over 50, and if there has been a long ulcer history with previous episodes of bleeding. If operation can be safely done at once, the patient is saved both the risk of further bleeding and the time spent on medical treatment, which he may well grudge if after a few weeks he has then to give more time for the resection of his ulcer. The operation, however, tends to be rather easier for the surgeon and safer for the patient if it can be held over till the ulcer has begun to heal well and the bleeding has stopped, so that if the diagnosis of chronic ulcer is not certain then the advantages of immediate laparotomy are less clear and the indication for operation is more uncertain. As a rule, if the haemorrhage continues, the history is suggestive of ulcer, and if the patient is over 60 immediate surgery is usually advisable, but the risks are certainly considerable (see below). A good blood bank and expert nursing are essential requisites.

Later Progress and Management

The stools should be watched for the disappearance of melaena, but if, as is advisable, iron is given early their colour will remain dark, even though the bleeding has stopped, and chemical tests must be utilized to show the presence or absence of blood. The bowels do not usually require any special attention for the first few days, when there is often some diarrhoea with offensive tarry stools. Later, constipation is usual—as may be the case from the beginning—and a weak soap enema may be given on the fourth or fifth day. At the same time a mild laxative such as liquid paraffin and magnesium hydroxide emulsion (*N.F.*, 1952), ½ fl. oz. (14 ml.) once or twice a day should be ordered. It is important to keep the bowels open at this stage, for the altered blood in the intestines is thought to cause pyrexia, which may be a source of anxiety and uncertainty, and, though it is possible that the temperature is, in fact, due to general metabolic changes in body proteins after haemorrhage, it nevertheless often settles after the bowels have been emptied. It is not always easy to decide when a barium-meal examination may safely be undertaken, but in most cases this can certainly be carried out within the first ten days. It is best to do the examination at the earliest moment possible, as the healing of an ulcer is often very rapid after a haemorrhage, and radiological examination two to three weeks after the bleeding has stopped may give an indecisive result. The dangers of early *x*-ray examination—within a few days of the bleeding—are slight and consist more in the risk of syncope and exhaustion of the patient than in the barium meal itself causing further bleeding, even though the radiologist may have to palpate fairly deep to demonstrate an ulcer satisfactorily.

Oral iron may be started from the beginning of treatment, and certainly within a week of the bleeding. Organic iron is more readily absorbed than inorganic, and not more than about 25% of such a salt as ferrous sulphate is, in fact, utilized by the body. Some preparation of ferrous gluconate, saccharate, or succinate is the most useful and least irritant, and it is estimated that about 30 mg. of iron in this form will raise the haemoglobin by 1%. Intravenous iron may be necessary but is not always easy to give; it is advisable only when there is extreme intolerance to oral preparations or the blood fails to improve after adequate oral dosage. A suitable oral preparation is ferrous gluconate, 0.3 g. three times a day. The official iron and ammonium citrate mixture very often causes gastric disturbance, as do the pills of ferrous sulphate unless specially coated to reach the intestine undissolved. Ascorbic acid should be given with iron as an aid to healing and to quicken the rate of recovery of the anaemia; the dose should be 200 mg. daily, or double this amount if the patient has for any reason been on a deficient diet before the haemorrhage.

Prolonged bed rest is not advisable after haemorrhage, and the patient may be allowed to get up for the commode from the beginning unless the bleeding has been very severe. He may go to the bathroom and sit in a chair for short periods as soon as his blood pressure has risen to a satisfactory level and the haemoglobin is above 60%.

In most cases he may be allowed out after three to four weeks, but the future treatment must, of course, be guided by the causative condition. The risk of post-haemorrhagic thrombosis is increased by long immobility in bed and can probably be lessened by early ambulation and the free administration of fluids.

Treatment of Oesophageal Varices

Oesophagoscopy will usually show the presence of varices, as may in many cases a barium swallow. Numerous methods of local treatment have been devised, including injection of the veins with sclerosing fluids, but none has given much success. Various operations designed to reduce portal tension of the porto-caval shunt type have been shown to reduce the varices in some cases, and ligation of the splenic artery has also been advocated, but with little to support it. Spontaneous disappearance of the varicosities is not unknown.

Prognosis

The risk of immediate death from haemorrhage is highest in cases of ruptured oesophageal varices secondary to portal hypertension, and it is a frequent mode of death in Banti's syndrome; in cases of cirrhosis over half the patients die within a year of the bleeding. In cases of haemorrhage from chronic peptic ulcer occurring in patients under 40 years of age death is rare; the risk is less than 1 in 20 amongst patients under 50, but rises to at least 1 in 10 in those over 60 and to about 1 in 5 in those over 70. In bleeding due to acute erosions death is also rare, even though the bleeding may be very severe, and the mortality in younger subjects is certainly not more than 1%. Loss of blood by vomiting is in general associated with a worse prognosis than when there is only melaena, perhaps because the loss is more rapid in the former case.

Next article on Emergencies in General Practice.—"Acute Respiratory Obstruction," by Mr. Norman A. Jory.

MANIPULATIVE METHODS IN ORTHOPAEDICS*

BY

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Cyriax (1955) has recently drawn attention to the fact that back lesions very often require manipulative treatment. He also mentions that members of the profession have actually recommended osteopathy to their patients (in spite of the G.M.C.'s warning notice).

My interest arose out of a chain of events. Not long after starting to do laminectomies for disk lesions I worked under a surgeon who regularly manipulated backs and necks under anaesthesia. He obtained very gratifying results without producing cauda equina lesions or other noxious sequelae. I then chanced to see a patient with recurrent low back pain and sciatica who was away from home and who showed me what her own doctor did to relieve her. I performed this rotatory manipulation quite gently and with the desired effect. Her symptoms and signs were what I regarded at that time as indicating a disk lesion. Thirdly, a young woman patient came to see me, complaining of pain in the back of the leg which was not severe unless she did certain things, but which had been present on and off for four years since a fall in which she fractured her eleventh dorsal vertebra. She had been treated in a plaster jacket for four months, so there seemed no point in trying this again. Physiotherapy and a corset were of no avail, so, wishing to avoid laminectomy if possible, I manipulated her under an anaesthetic. She lost her pain completely, but only for a week. After further trial of other methods without relief I did it again, with the same result. After the third manipulation, which again relieved her for a short time, it became clear that if she was to be treated by manipulative methods it must be done without anaesthesia. By repeated manipulation at slowly increasing periods she was eventually relieved completely and has since been able to do bending work without pain, even over prolonged periods.

I started manipulating other patients, and found that by these measures I could relieve some in whom other methods short of operation had failed. I also found some surprising results, including the complete relief of a pain localized to the inner side of the knee and associated with some limitation of extension. The more I manipulated the better my results, but there were still failures, and I was interested when one or two of these patients let me know later that they had been cured by osteopaths.

I decided that I must learn more about osteopathy, in spite of my early indoctrination against it, and by chance I met a qualified doctor now practising osteopathy in London. I spent a week seeing his patients with him, and very quickly realized that there was a lot that I could learn from him. I emphasize that I am not an osteopath but an orthopaedic surgeon.

A Fresh Approach to Back Pain

The first thing that surprised me was the way in which he examined a back. He tested each and every joint for movement and tenderness. When he found a stiff joint he examined it for position. I was also surprised to learn that the sacro-iliac joint is a mobile joint and that when stiff it is frequently the cause of symptoms. I was intrigued to learn a simple method of testing for its mobility.

Having been shown the technique of localized spinal examination, localized treatment was the logical sequel, and I was quickly shown a variety of methods. The principle is that the joints above and below the one to be manipulated are "locked" by positioning, and force is then applied to the joint, either directly or by using the locked spine as a lever. Needless to say, it is most important that the joint should be moved in the right direction.

Until this visit I had never used manipulation on patients with recent acute back pain, but there seemed to be no definite dividing line, and when I asked I was told that even the most acute cases would respond very well to this treatment. I have since proved this amply to my own and the patients' satisfaction.

What, then, is the acute incident that happens to produce a sudden attack of, say, "lumbago"? Surely not a displacement backwards of a piece of softened disk material (but see Cyriax, 1955). The pressure on the disk in flexion is said to be very high, and if a pathway has been made by a protrusion of disk material there is no doubt in my mind that even if it can be replaced it must protrude again as soon as the spine is flexed. Cyriax (1955) agrees that manipulation can cure these patients. I believe that the cause of the pain is to be found in a derangement of the zygapophysial joints and that this derangement is mechanical in nature. The pain may result from stretching or pinching of the capsule or of adhesions, or from reflex muscle spasm round the deranged joint.

What is a disk protrusion, and what has it to do with the joint lesion? I think this conception of the initial pathological process can perhaps throw some light on problems that have so far been obscure.

The intervertebral disk has no blood vessels: it has only lymph channels. The method of nutrition appears, therefore, to be by an osmotic pump. The osmotic pressure of disk material is high, and with the spine at rest fluid is sucked in. In the erect or, still more, in the flexed position fluid is squeezed out by a rise in the hydrostatic pressure. If relative motion of the vertebra above and below is prevented by the joint derangement and the muscle spasm round it, the pump cannot work and the disk receives no nutriment. Softening follows, and maybe protrusion.

On this theory the degeneration of teen-age disks as well as the delay often seen between injury and protrusion can be explained. This restriction of motion in the zygapophysial joint is the so-called osteopathic lesion.

It is now widely recognized that intervertebral joint derangements can cause dysfunction in somatic nerves, and it seems illogical to deny that the autonomic nerves can be similarly affected. If, however, one admits this the field of possible secondary symptoms is very much widened.

One difficulty in theorizing about the sacro-iliac joint is to find any explanation of the sites to which pain is referred in derangements of this joint. In my experience pain is referred principally to the back, to the groin and perineum, to the inner side of the knee, or to the heel. Sacro-iliac joint derangements are often accompanied by circulatory changes in the leg, which strongly suggests some involvement of the sympathetic.

One of the main reasons for having a mobile spine is to permit the eyes to be turned quickly to any direction. This function involves complicated interaction of spinal joints and muscles. If a joint becomes stuck in other than its normal position compensatory alterations of position of joints at other levels take place. In time this can lead to the production of secondary joint lesions. Lesions in the sacro-iliac joints can be either primary or secondary. The former is the common cause of acute pain in the back and leg after parturition. The latter very commonly follows lumbar joint derangements.

When considering spinal balance it is clearly of interest to know if the legs are equal in length. It follows that a

*A paper delivered to the Gloucestershire Branch of the British Medical Association on January 13, 1955.

constant unilateral strain is thrown on sacro-iliac and low lumbar joints if the legs are uneven. It is very surprising to find how many patients with back trouble have legs that are unequal by more than ½ in. (0.3 cm.), and it is equally surprising to find how much some patients' symptoms are relieved by partial correction by a heel lift.

It is clearly insufficient to measure with a tape from the anterior superior spine. The error due to movement of the sacro-iliac joint may be more than ½ in. (1.3 cm.). Examination of both anterior and posterior superior spines in the erect position, with assessment of the heights of the iliac crests, gives a useful clinical appreciation. The only accurate method is to have the pelvis *x*-rayed with the patient erect and with the feet together and the knees straight. If the cassette holder is adjusted to the horizontal the relative heights of the femoral heads above the lower edge of the film give the difference.

One other structure of the effects of which the explanation is obscure is the sacro-tuberous ligament. This ligament, of course, is one of those bridging—at a distance—the sacro-iliac joint, and is commonly found to be thickened, tense, and tender in patients with chronic low back pain. I do not know what the pathological process is, but if the ligament is pressed on for upwards of half a minute it gradually gives way and in the process an aching pain is often felt in the leg or in the back. Personally I use the technique although I cannot explain its effects, because I find it helps some patients very much.

Methods of Diagnosis

The spine is usually examined erect first. Leg inequality is looked for, the relative positions of the anterior and posterior superior spines is observed, and the mobility of the spine examined in flexion, extension, and side-bending.

The usual neurological examination is then made, but in addition the mobility of the sacro-iliac joints is tested with the patient supine. This is done by using the leg as a lever. When the leg is externally rotated with a little flick with the knee flexed by about 60 degrees and the hip abducted by about 30 degrees the innominate is moved posteriorly on the sacrum. The reverse movement is obtained by internal rotation in neutral abduction and almost full extension. If the sacro-iliac joint is mobile the leg becomes apparently longer and shorter as the first and the second movements are made. The shift should be at least ½ in. (1.3 cm.), and is best observed by comparing the levels of the medial malleoli before and after each movement.

If one sacro-iliac joint is stiff it is essential to discover what its position is. The relative levels of the superior spines have been examined already for this purpose, but confirmation can be obtained from the relative prominence of the posterior superior spines in the prone position.

The patient is then laid on the side and the upper leg is fully flexed at the hip and knee. The examiner uses his abdomen to control the leg, flexing and extending gently while palpating the interspinous intervals with the fingers. By this means it is possible to determine exactly which joints are mobile and which stiff. Interspinous tenderness is also elicited. When the stiff joints have been found the position of the joint can be determined by palpating the transverse processes with the patient still in the lateral position. The transverse process of a bone that is causing trouble will be made more prominent not only by its rotation but by the tender area of muscle spasm over it. If it cannot be felt on the one side the patient is turned over and the examination repeated on the other side.

The joints of the dorsal spine are most easily examined in the sitting position with the legs over the edge of the couch, the hands linked behind the neck, and the elbows together. The patient bends forwards, resting loosely on the forearm of the examiner, who palpates the interspinous interval with the fingers of the other hand. The determination of position is most easily done prone, when with the flat of the finger a bar of what is apparently muscle spasm can be felt overlying the transverse process, and of course rib, on the side that is displaced posteriorly.

The neck is examined in the same position with the examiner standing behind the patient and the forehead supported in one hand while the other palpates the interspinous intervals. In all these procedures it is essential that the patient should relax in order to allow whatever free movement is possible. The rotation in the cervical region is determined by palpating the transverse processes, and can be done sitting, supine, or prone with the head flexed.

Radiographs are, of course, essential in almost all cases, particularly to determine unsuspected bony abnormalities and leg length. As, however, every joint in the back is examined, the likelihood of missing infective or neoplastic processes is much less than with the orthodox type of examination.

Treatment

The basis of treatment is the replacement into its more normal position of any bone that is causing symptoms as a result of its displacement. It is therefore essential first to know which bone is displaced and in which direction. If a bone is pushed further into the wrong direction the joint is strained more and the symptoms can be made much worse.

The intervertebral joints lock in certain positions, so that they cannot be strained. Full flexion and full extension are the simplest, but are not always suitable. Side flexion with rotation also locks the joints and is most useful. A valuable technique for the lumbar spine is performed thus:

The patient is in the lateral position with the lesion uppermost. The upper part of the body is raised by pillows or by raising the end of the couch, and the shoulder is pushed backwards until the tissue tension can be felt to indicate that the joints above the lesion are locked. The leg is then flexed on the trunk until the tension can be felt to come up to the lesion from below. A thrust forwards on the transverse process then completes the manipulation when combined with a slight exaggeration of the backward rotation of the shoulder and of the flexion of the hip. Thus the upper part of the spine is locked by side flexion and rotation, the lower by flexion. In all these procedures the thrust should be of high velocity but low amplitude, a sharp thrust that is stopped almost as soon as it has begun.

The accurate perception of tissue tension is probably the most difficult part of the whole technique for the beginner to learn. It is essential, and until the art is acquired many patients will suffer unnecessarily, often without receiving any benefit.

Description of other techniques is beyond the scope of this paper.

Results

I regret that I have as yet no figures, and I cannot possibly claim not to have any failures. I am satisfied, however, that my results are much better than they were by orthodox methods alone. I still use physiotherapy, supporting garments, and occasionally plaster jackets for selected cases.

Of particular interest are certain somewhat surprising results, one of which I have already referred to—namely, pain on the inner side of the knee due to sacro-iliac joint derangement. This is often associated with some limitation of extension and a synovial effusion. It forms a most important differential diagnosis of torn medial meniscus because it is very common. I believe it to account for most of the negative explorations of the inner side of the knee-joint. The differential diagnosis can usually be guessed at on the history alone, but unfortunately some patients date the trouble accurately to an injury when "something went click in my knee." The injury is not usually such that one would expect a meniscus tear, and I presume the explanation to be that the click arose in the sacro-iliac joint but was thought to come from the knee because it was to the latter joint that the pain was immediately referred. The treatment is to manipulate the sacro-iliac joint, and the expression on the patient's face is worth watching when the knee will extend fully after the back alone has been treated.

The frozen shoulder is another condition that I have found can be relieved or, if seen in time, aborted. The

joint which is most constantly deranged in this condition is that between the second and third dorsal vertebrae. There is always associated cervical trouble, but I have been driven to the conclusion that trophic changes from sympathetic dysfunction are the prime cause.

Tennis elbow is usually associated with lesions in both dorsal and cervical regions, but for some reason the less localized variety with pain extending to the fingers seems easier to cure.

Migraine in a high proportion of cases, as well as much headache, is associated with upper cervical joint derangements, and can be relieved by their treatment. Disturbance of the sympathetic control of the vertebral artery is a possible mechanism.

The Psychological Factor

Many patients with back pain have a hysterical overlay. This has only too often been encouraged by the well-meaning but misguided remarks of our colleagues who have been unable to find the cause.

Only in a very small proportion is the overlay not relieved by successful treatment of the physical cause.

I can add my own experience of the debilitating effect of chronic back pain. I have had it, and I would recommend it as a very useful lesson to those who would treat the condition in others.

REFERENCE

Cyriax, J. (1955). *British Medical Journal*, **1**, 140.

VOLUNTARY SERVICE FOR STATE HOSPITALS

The annual meeting of the National League of Hospital Friends, held in London on March 9, was addressed by Lord Beveridge, who was elected president at the meeting, and by Mr. Iain Macleod, M.P., Minister of Health. Mr. Percy Wetenhall was in the chair.

LORD BEVERIDGE said that the League concerned itself not only with helping hospitals and their patients but with patients suffering from chronic illness who were or could be treated in their own homes. It did so, not merely to save expenditure on hospitals, but because such patients, given reasonable home conditions, were likely to be much happier in familiar surroundings. The problem was to extend the possibility of medical and nursing treatment outside the hospital by means of assistance of various kinds. He appealed to women who were not fully occupied otherwise to serve as home helps. The problem of the chronic sick, with which was linked the problem of the infirm aged, was assuming larger and larger dimensions. In another quarter of a century there might well be ten million old people in this country. The need for help for such people, not only in household jobs but in the provision of companionship and occupation, would become more and more pressing.

The general practitioner, Lord Beveridge continued, had a great part to play in all this. If he could be made responsible for seeing that these domiciliary patients not only had the necessary medical and nursing care but everything else for their comfort and welfare, in which the co-operation of the local authority might have to be enlisted, it would be an ideal arrangement. Notwithstanding the existence of the National Health Service there remained a wide sphere for voluntary action, the great merit of which was that it was not tied down by regulations and Acts of Parliament.

The MINISTER OF HEALTH, in a brief speech, said it was not known exactly how many Leagues of Friends existed in the hospital world, because many were not affiliated with the National League and many hospitals had such voluntary bodies but working under other names. He was sending out a questionary to the heads of all hospitals in the country in order to find out exactly how much voluntary effort was going on, and the Ministry would not be content with progress in this field until every hospital had its own local body of devoted voluntary helpers. His impression was that they were much nearer the goal than might be supposed. Whenever he visited a hospital in any part of the country he made it a rule to ask about the associated voluntary effort, and it was very unusual to find a hospital which had not some organization of this kind. It had been suggested to him that he might send out new instructions to hospitals about enlisting voluntary service, but he did not think that much could be done by circularization; it must be left to local initiative.

One of the great opportunities for service still open in the field of voluntary effort, said Mr. Macleod, was in the treatment of the chronic sick, and it might be that the Leagues of Hospital Friends could do something to mitigate the difficulties in providing home helps and in assisting in general domiciliary treatment. The treatment of the mentally sick found us still in many ways out of date in our thinking and in our laws. There was still amongst unenlightened people an attitude towards the mentally ill that they must do all they could to change. There were special difficulties because mental hospitals were sometimes remote and difficult of access, but they must not rest content until mental hospitals no less than others were covered by "friendship." The Leagues should set themselves not to supplant but to supplement other agencies, such as the Red Cross and St. John and the W.V.S. They should not be too precise in their work. For example, a hospital might be prevented from providing some amenity because it had to install new treatment facilities, and it was here that the Leagues of Hospital Friends came in.

Nova et Vetera

DR. EDWARD HARRISON, OF HORNCASTLE, AND THE LINCOLNSHIRE MEDICAL BENEVOLENT SOCIETY*

The year 1954 marks the 150th anniversary of the foundation of the Lincolnshire Medical Benevolent Society. The society owes its origin to the indefatigable zeal and crusading spirit of a pioneer medical reformer, Dr. Edward Harrison, of Horncastle, Lincolnshire. Born in Bankfield, Lancashire, in 1766, of an old Lancashire family, he qualified in Edinburgh, and practised medicine for many years in Horncastle (later in London), and became an outstanding figure in the history of medicine, whose fame extended far beyond the boundaries of the county.

In 1820 he published a treatise† on "Remarks upon the different appearances of the back, breast, and ribs, in persons affected with spinal disease, etc." He wrote various other works during his lifetime, and his main interest was clearly in orthopaedics. He survived until his 79th year—no mean achievement for the times—and the medical tradition of the family was carried on by his nephew, Richard Harrison.

Edward Harrison's interests were not by any means wholly confined to medical reform and orthopaedic surgery, for he carried on a busy general practice, and was one of the honorary physicians of the Horncastle Dispensary, founded in 1789. Horncastle in those days was a thriving and important country market town, as readers of George Borrow will recall.

In addition to these other activities Dr. Harrison maintained a large house in West Street, Horncastle (still used as a doctor's residence), and, finding it unnecessarily commodious for his needs, he conducted there a small private mental asylum. He seems to have been a man not only of catholic medical interests but also of indefatigable energy. In the opening years of the nineteenth century he devoted much of his time and characteristic zeal to a crusade designed to raise the status of the medical profession, which had fallen to a low ebb, particularly in the remoter provinces.

*Extract from an address delivered by Dr. Allan H. Briggs, Mayor of Lincoln, at the 150th Anniversary celebrations.

†His name thus became associated with Harrison's grooves or sulcus, but it is now contended (see Naish, J., and Wallis, M. R. E., *British Medical Journal*, 1948, **1**, 541) that the grooves were first described by Dr. Edwin Harrison (1779–1847), physician to the St. Marylebone Infirmary.

Quackery was rife; the qualified practitioner earned a precarious living in competition with a host of accoucheurs, apothecaries, druggists, and medical pretenders of every kind; there were no adequate standards for such remedies as were available, and medicines were unreliable and frequently adulterated. He wrote, "It appears from authentic documents that the regular faculty do not constitute one-ninth of the practitioners now occupying physic for emolument in the County of Lincoln, and that besides the errors and unintentional injuries which are daily committed by ignorant quacks upon their too credulous patients there is great reason to fear that some of them acquire large sums of money and do irreparable mischief to many pregnant women and their harmless offspring by trying to relieve the former from the natural consequences of their indiscreet and unauthorized familiarities."

The early records of the Lincolnshire Medical Benevolent Society were to show all too clearly what a laborious and hazardous occupation the practice of medicine and surgery was in those days of primitive transport, ignorance, and penury. The chance of accident or disease might quickly reduce the most successful doctor to distress and want; there was often little margin.

Dr. Harrison set about tackling these problems energetically: he determined upon the foundation of a benevolent society. He prepared a comprehensive set of rules and an "Address to the Public," which he circulated among those likely to be interested, and the first recorded meeting of the society (at which he was not unnaturally elected president) took place at the Bull Inn, Horncastle, on September 21, 1804. Some twenty founder members attended, and the preparatory work had been so well done that a substantial sum of money (£53 13s.) was already in hand. To overcome the formidable travelling difficulties the county was divided up into districts under the charge of vice-presidents, and this valuable feature of the society is still preserved, although sound finance and improving communications have rendered it necessary for the charitable work of the society to be transacted through an annual anniversary meeting, which has travelled round the country from year to year for the past century and a half.

Although the primary function of the society was benevolent Dr. Harrison had other ideas in mind: he saw in it an invaluable means of furthering his ambitions for medical reform, and also the makings of a professional society where members might hear and read dissertations on medical topics.

These multiple objects proved too much to achieve at a single stroke: medical reform was to come—the Anatomy Act of 1832, the Registration Act of 1838, and the Public Health Act of 1848. How far local agitation in Lincolnshire (and elsewhere) contributed to these measures is difficult to estimate, but the indirect influence may well have been considerable. Medical reform thus gradually dropped out of the society's affairs, and the formation of the British Medical Association (1832) and the Lincoln Medical Society (1864) covered many other purposes which Dr. Harrison had sought to serve before his time.

The benevolent functions of the society have, however, gone on from strength to strength, surviving the changes and chances of succeeding generations: the old minute-book reflects the passing of the horse chaise as a means of transport and the introduction of the railway; it saw the introduction of the penny post; it was begun before Waterloo and goes on after two world wars without interruption. Benefactions in ever-increasing volume have been a regular feature of the anniversary meetings, and the annual disbursement from subscriptions and investment income average over £300. During the first century of its life the society dispensed over £7,000, and, during the last fifty years, over £10,000 more.

This long tale of generous assistance to impoverished or disabled medical men, and to their orphans, widows, and dependants, forms a fine and impressive memorial to a great doctor, pioneer reformer, and medical visionary born before his time: Dr. Edward Harrison, of Horncastle.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Post-maturity and Breech Presentation

SIR,—Until recently post-maturity was one of the most controversial subjects in obstetrics. The majority of obstetricians will now agree that this controversy ended when James Walker[1] published his work in 1954. He showed that the oxygenating capacity of the placenta rapidly diminishes after the 40th week; by the 43rd week there is hardly any reserve in the oxygen supply to the foetus. It is therefore much easier to kill the foetus at 43 weeks. He also produced clinical evidence that the stillbirth rate at Aberdeen was far greater when the foetus was post-mature, and he quoted Gibberd's similar findings at Queen Charlotte's. In both cases all deaths where disproportion or some other factor contributed to the result were excluded. Unfortunately, this valuable work has not yet reached the more widely read medical journals. Furthermore, when this dangerous complication coincides with a breech presentation, the risk to the foetus is indeed very considerable. The danger of intracranial injury from too rapid delivery is continually being stressed, and quite rightly so. The danger of too slow delivery must be almost as great when the placenta has diminished in efficiency and the oxygen supply to the foetus is only just enough to maintain its life before the delivery of the trunk. Following the delivery of the trunk, when the oxygen supply must be almost completely cut off, such a foetus cannot possibly survive if there is a delay of minutes.

There have, of course, been many obstetricians in the past who appreciated the danger of post-maturity. Yet until a year ago no authoritative textbook was prepared to admit that post-maturity constituted a danger in itself. There would appear to be two reasons for this. First, most obstetricians have at some time or another seen a satisfactory result despite an abnormally long gestation. Some placentae, like human beings, are capable of functioning efficiently well beyond the average allotted span. Secondly, there is a tendency to reason that, when a placenta is so degenerate that it cannot maintain the life of the foetus, neither will it produce an adequate amount of the hormones which are necessary for pregnancy to continue. The foetus is thus saved from death by the mother going into labour and expelling it from the uterus. This quite likely is true in the majority of cases, but not in all. It must be remembered that the maintenance of foetal life is dependent on a sufficiently large area where foetal and maternal blood are in intimate relationship, whereas an adequate production of hormones is dependent on a sufficient number of secreting cells. It is obvious, therefore, that occasionally extensive infarction may result in an insufficient area where foetal and maternal blood are in intimate contact for satisfactory oxygenation to take place and yet the production of hormones is sufficient to continue pregnancy.

This communication is prompted by a recent case where the writer was called to deliver a breech in a primigravida aged 35, and she was three weeks post-mature. The mouth was exposed within five minutes of the birth of the breech, and yet the foetus made no attempt to breathe. I am certain that this foetus died of asphyxia. The management of breech deliveries, more than most obstetric operations, depends on the skill of the attendant; the object of this letter is merely to stress the added risk to the foetus when the pregnancy is also post-mature.—I am, etc.,

London, N.W.1. E. ROBERT REES.

REFERENCE

[1] *J. Obstet. Gynaec. Brit. Emp.*, 1954, **61**, 162.

Anaesthesia and Cortisone Therapy

SIR,—The introduction of cortisone and related drugs into general medical practice has brought with it further hazards for the anaesthetist. It may not be generally known that patients on cortisone therapy are sensitive to anaesthetic agents; this is particularly true of opiates and barbiturates.[1] Moreover, such patients tolerate blood loss badly, and Fraser *et al.*[2] have reported the death of a patient from post-operative shock in spite of normally adequate therapy.

It has been stated[3] that all patients who have received cortisone therapy within six months prior to the proposed date of operation require special preparation. We would endorse that view, and would suggest that all patients should be asked specifically about cortisone therapy and, where indicated, the necessary preparations carried out. The pre-operative management of these patients has already been adequately described by Pender.[3]—We are, etc.,

F. G. WOOD-SMITH.
J. P. PAYNE.

London, W.12.

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2 *J. Amer. med. Ass.*, 1952, **149**, 1542.
3 Pender, J. W., *Wis. med. J.*, 1954, **53**, 215.

Standards of Fitness of Commercial Vehicle Drivers

SIR,—Dr. Josefine Webb (*Journal*, February 26, p. 515) draws attention to the need for improvement in certain medical aspects of the present system of granting driving licences to professional drivers. Some months ago, however, the Association made recommendations to the Ministry of Transport and Civil Aviation for this purpose.[1]

Dr. Webb has fallen into the trap of failing to compare like with like. The medical reasons for rejection of men for military service do not necessarily bear any relation to their safety as drivers; severe flat feet may indeed be a good reason for driving. It is also possible that many of the drivers whose papers were examined by Dr. Webb had declared their defects on the application form and had nevertheless been issued with a licence. The responsibility for issuing licences lies not with the applicant but with the licensing authority. The applicant's responsibility is limited to a declaration (under severe penalty) of his defects. Over three million driving licences of different kinds are issued annually, and until some new method emerges of taking medical histories on a large scale the statutory declaration will have to serve.

The pride of many public service drivers in their safe driving awards is fully justified. I wonder how many of us could maintain the accident-free record which many of these men do for 20 or more years of several hours' driving a day?—I am, etc.,

LESLIE NORMAN.

London, N.W.1.

REFERENCE

1 *British Medical Journal Supplement*, 1954, **1**, 117.

Septic Injuries in Industry

SIR,—Your leading article (*Journal*, March 5, p. 591) on septic injuries in industry refers to work done in 1949 and 1952 on the incidence of penicillin-resistant forms of *Staphylococcus aureus* in infections of the finger, and remarks that "more recent bacteriological studies are not available."

It may help if I refer to a letter written to one of your contemporaries last December.[1] In it I reported that the casualty department at Sunderland Royal Infirmary has carried out a sample "bacteriological survey" of this problem every year since 1950. As recently as the date of that letter we have been able to confirm that there is no significant increase in penicillin resistance in these infections, provided that the examination is made on closed lesions at the time pus is first obtainable. Discharging lesions show a higher incidence of penicillin-resistant forms than closed lesions, but they show also a higher incidence of gram-negative organisms, so that it is probable that many antibiotic-resistant staphylococci in discharging lesions are the result of secondary infection in medical or nursing clinics.[2]

There is, I believe, always a certain incidence of resistant forms in any series of staphylococcal infections, and it is possible that there always has been. This incidence is somewhere between 5% and 10%.[3] In this area, at least, we have no evidence that it has materially increased in the last five years. The degree of resistance is usually not very high (0.16 to 0.4 U. per ml. *in vitro*), and these cases also almost always respond to a very short course of penicillin administered in large doses, combined with surgical intervention as soon as there is an indication for it.

Your leading article very rightly emphasizes the cost to individuals and to the community of this type of minor sepsis. We estimated that the annual cost to the Exchequer in sickness and injury benefit of all cases attending casualty departments is (by pure coincidence) about £1 per new case annually. Our own department sees about 15,000 cases, and a rough estimate of the cost of disability comes to £15,000. To reduce this disability by 10% repays the expense of enlisting experienced skill in treatment, and in many clinics it can be reduced by much more than 10%.—I am, etc.,

THOMAS G. LOWDEN.

Dublin.

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Sudden Death in Labour

SIR,—While the cause of death in the case described by Dr. Patricia E. Campbell (*Journal*, January 8, p. 87) may have been due to amniotic embolism or, as Mr. R. C. Bell suggests (*Journal*, February 19, p. 480), accidental intravenous injection of the procaine penicillin, there seems to be ample evidence that penicillin itself can cause anaphylactic shock.

In a review of eight cases of anaphylaxis and death following shortly after the administration of penicillin, Rosenthal[1] concluded that, because of the diversity of the types of penicillin used in these cases, no one type of penicillin could be regarded as the sensitizing antigen, and that penicillin *per se* must be regarded as the antigen.—I am, etc.,

W. O. THOMSON.

Glasgow, C.2.

REFERENCE

1 *N.Y. St. J. Med.*, 1954, **54**, 1485.

Anaphylaxis After Procaine Penicillin

SIR,—Dr. Patricia E. Campbell reported a fatal case of anaphylaxis following an injection of procaine penicillin (*Journal*, January 8, p. 87) and Mr. R. C. Bell queried the cause of death in this case in a letter (*Journal*, February 19, p. 480). This correspondence prompts me to report the following case, which, although fortunately not fatal, leaves no doubt that procaine pencillin can produce alarming anaphylactic reactions.

The patient, an obese woman aged 42, had a history of rheumatism and recurrent attacks of bronchitis. She had a moderate degree of mitral stenosis, fairly well compensated. In August, 1953, she was admitted to hospital for bronchitis with cardiac strain. She was given a course of crystalline penicillin with good results. In October, 1954, she developed bronchitis and was treated at home with six daily injections of "distaquaine" suspension (300,000 units daily), again with good results. On February 2, 1955, the patient was seen at home again suffering from bronchitis with pyrexia: heart regular. She was given distaquaine suspension 300,000 units intramuscularly, and the usual precaution was taken of attempting to withdraw the piston to ensure that the needle was not in a vein. About 10 minutes later the doctor was asked to call at once as it was thought that the patient had died.

On arrival the patient was found to be in an alarming condition. She lay flat on her back, cyanotic, covered in sweat, and gasping for breath. Her pulse was not perceptible at the wrist, but auscultation of the heart revealed marked tachycardia with very faint sounds. The end of the bed was raised and an intramuscular injection of adrenaline hydrochloride 1/1,000 was

commenced, 2 ml. being administered over a period of 15 minutes. Gradually her condition improved so that she could be propped up in a sitting position, and at this point auscultation of the chest revealed sibilant rhonchi and moist rales throughout both lung fields. The patient was by this time able to drink some hot sweet tea which had been optimistically ordered up at the commencement of the adrenaline therapy. She complained of substernal tightness plus difficulty in breathing. Two hours later the patient's colour had greatly improved, her pulse was of good volume, and there was less evidence of pulmonary congestion. A few days later she was quite well and her bronchitis had cleared up.

The rapid onset of the reaction following the injection, with the collapse, cyanosis, sweating, and gasping for breath, is surely typical of anaphylactic shock. Accidental intravenous injection can be ruled out in this case. Whether the reaction was caused by the penicillin or by the procaine could not be determined, as the patient was unwilling to be subjected to an intradermal injection of 0.1 ml. of 1% procaine hydrochloride solution. Her reluctance is quite understandable considering her recent experience.—I am, etc.,

Peterborough. DAVID C. WRIGHT.

Whither Natural Childbirth?

SIR,—Dr. Constance L. Beynon, in her letter "Whither Natural Childbirth?" (*Journal*, February 19, p. 475), seeks to halt the trend towards wider provision of preparation for childbirth. She states that "to any other generation" special training for childbearing "might seem absurd"—an argument which will carry little weight when we recall the attitude of other generations to analgesia and asepsis in obstetrics. Perhaps the term "natural childbirth" contributes to the confusion by implying something we cannot hope or wish to recapture as civilized, social beings. For civilized people, however, "painless childbirth" would seem an appropriate aim, although not always to be realized at present. This phase, however, appears to arouse Dr. Beynon's wrath, for she apparently hopes to wean women away from demanding it. As she seems to deny, by implication, the possibility of achieving painless childbirth, I feel justified in quoting my own extremely limited experience in general-practitioner domiciliary obstetrics, without claiming any special knowledge and recognizing that so small an experience presents nothing that a statistician need bother to read, let alone disprove.

It is my practice to give my patients a brief series of talks in the latter months of pregnancy, the total time taken being a little over an hour. In them, I explain the course and sensations of labour, encourage an attitude of interest and participation, rather than of resignation, and give instruction in the art of conscious physical relaxation and of rhythmical breathing for the first stage, and in deep breath-holding for the second stage. Nobody, of course, attempts to give a "balanced grasp of midwifery" in such classes, and it is absurd to suggest that they do. Once labour is well established, I remain with the mothers and assist them to apply what they have learnt. Although working in all sorts of homes and with midwives giving varying (but increasing) co-operation, I feel justified in promising mothers treated in this way that their pain will be diminished considerably in nearly all cases and entirely abolished in some.

The experience of the last 12 mothers whom I have prepared and delivered is summarized as follows. Three cases (1 primipara, 2 multiparae): no pain at any stage. Three cases (all multiparae): moderate pain for less than 10 minutes at the end of the first stage. Four cases (all multiparae): moderate pain for up to half an hour, one taking gas-and-air, another wishing to for one very painful contraction, but it was not available. One multipara had backache for about one hour, but did not want gas-and-air. One primipara, while maintaining excellent control and relaxation, required pethidine and gas-and-air for the latter three hours of the first stage.

While this method of preparation and conduct of labour undoubtedly does aid morale (and I cannot see that the maintenance of morale should be regarded as extravagance) it is not merely a case of instilling fortitude; rather it is a means of suppressing pain so that powerful uterine contractions, while still causing a powerful sensation, are not painful. As regards the many experts who find no influence on length of labour, complication rates, etc., I believe that one cause for this lies in the gulf which usually separates the antenatal class from the labour ward. It is still rare for labour ward staff to have the time, interest, or knowledge to assist mothers to apply their methods, and few mothers are able to retain control without encouragement. The experience of the Paris polyclinic "Pierre Rouquès," where great stress is laid on labour ward support, has been definite in finding a reduced duration of labour, a reduced complication rate, and improved neonatal health.[1–4] In a recent paper on methylpentynol in labour, Bourne[5] showed how this drug allays anxiety and facilitates relaxation, and comments that labour in these cases is often speeded up. This statement has caused no adverse comment; why, then, should we be surprised if the alleviation of anxiety by explanation and assistance, combined with instruction in relaxation (a more physiological approach), has similar effects?

As regards the second stage of labour, it is true that bearing down, like defaecation, is a reflex act. Unlike defaecation, however, this reflex is often distorted by fear, panic, fatigue, and the influence of drugs. Antenatal explanation and training in deep breath-holding ensures that when this second stage starts the mother bears down more quickly and more efficiently, which, in turn, ensures freedom from pain and normal progress.

Dr. Beynon is concerned at the sums of public money being spent on antenatal classes. Questioning hospital patients leaves little doubt that the consumer in this case appreciates the efforts made. I believe there may be a case for simplifying and shortening the preparation, and I am certain that the full effect of preparation on the course of labour will only be achieved when labour ward management is based on the principles of the classes. Meanwhile, I hope no false consideration of economy will halt a development which I believe to be both humanely and medically desirable.—I am, etc.,

London, N.W.5. ANTHONY RYLE.

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3 *Revue de la Nouvelle Médicine*, 1954, No. 3, special number.
4 Ryle, A., *Med. Wld (Lond.)*, 1954, **80**, 36.
5 Bourne, G., *Lancet*, 1954, **2**, 522.

The National Formulary, 1955

SIR,—It is clear that the criticism of certain aspects of the *National Formulary 1955* voiced in your leading article (*Journal*, February 12, p. 402) was misdirected. The writer ascribes to the *Formulary* the function of helping practitioners to develop "sensible, honest, logical, and economical prescribing habits." Dr. W. N. Leak, writing with authority as a member of the joint committee which revised the *Formulary*, deplores this attitude in the *British Medical Journal*, and is at pains to point out in his admirably frank letter (*Journal*, February 26, p. 541) that no such consideration guided the members of the committee in their task (the strongest corroborative evidence for this view is surely to be found in the arrangement of the book). Instead, it seems that the committee's aim was to produce a documentary report on the pattern of prescribing observed in this country during the first half of the present century. They evidently regard the gratitude of the social historians of the future as a more fitting reward for their labours than the ephemeral applause of their contemporaries. The practitioners who confided to Dr. Leak their fear that the *Formulary* "is in some way an attempt to direct their prescribing" had no reason to be apprehensive.

Dr. Leak does well to remind us of the classical experiments of Chassar Moir, which vindicated the ergot alkaloids; and he has the intellectual courage to deduce from this episode that no reliance is to be placed on contemporary opinion of the therapeutic merits of drugs. His defence of the readmission to the *National Formulary* of mist. ammon. et seneg. (which he translates for the *in-illuminati* as ammonia and senega mixture) is not based on such uncertain ground, but on the incontrovertible evidence supplied by the experience of "three generations of doctors and patients." The most hardened sceptic who could do no better than cite the contrary experience of *two* generations of academic doctors would clearly be outmanned.

Dr. Leak takes a cautious view of the modern tendency to prescribe tablets, but is tantalizingly vague about the nature of the "overpowering burden" which this places on the

prescriber. Can he mean that, tablets being more portable than mixtures, the practitioner may be tempted to carry them in his bag? Or does he refer to the strain which is imposed on the memory by "tab. digoxin." as compared with, say, "mist. pot. brom. et valerian."? The "added expense to the State" which he mentions as a consequence of the practice is also hard to understand, since the dispensing fee charged for tablets is approximately half that for liquid preparations.

None will dispute Dr. Leak's contention that the use of bottles of medicine allows "flexible control" of dosage. The range of individual variation in volumetric capacity of domestic measures like "teaspoonfuls" is so wide that dosage is not so much "flexible" as speculative. It is readily conceded that the therapeutic effect of mist. ammon. et seneg. is largely independent of the size of dose administered. But would Dr. Leak agree that certain other drugs demand accurate rather than "flexible" dosage? I offer for his consideration digitalis, which has been well spoken of by at least eight generations of doctors and patients.—I am, etc.,

Edinburgh, 3. T. W. G. KINNEAR.

Encephalo-trigeminal Angiomatosis

SIR,—Of all the names suggested for the Sturge-Weber-Kalischer syndrome the best up to date seems to me that which I have lately heard of—namely, the "encephalo-trigeminal angiomatosis." There can, I think, be no doubt that both the encephalic and the facial constituents of the syndrome belong to the class of haemangiectatic hamartomatous errors of tissue development roughly grouped together as haemangiectatic naevi. But the area of face involved is not always limited to the trigeminal region of one side. The haemangiectatic abnormality of development may sometimes, in various degree, involve both sides of the face and indeed portions of both sides of the body.

In spite of the coexistence of various concomitant features in most typical cases, such as congenital glaucoma on the side of the encephalic lesion, and hemiparesis of the limbs of the opposite side of the body, I think that encephalo-trigeminal angiomatosis, or better still encephalo-facial haemangiomatosis, is the best term for the developmental syndrome in question.—I am, etc.,

London, N.W.1. F. PARKES WEBER.

Positive-pressure Respiration in Bulbo-spinal Poliomyelitis

SIR,—The interesting and detailed article by Drs. J. R. Harries and W. E. Lawes (*Journal*, February 19, p. 448) prompts me to record four similar cases treated by intermittent positive-pressure respiration (I.P.P.R.) in the poliomyelitis unit of the Rush Green Hospital during the past year. They were a girl of 11 years who recovered, and three males, aged 6, 24, and 28 years, all of whom died. In all four cases tracheotomy was performed under local anaesthesia and I.P.P.R. was carried on with the Beevor (mark I) respirator. Despite the obvious shortcomings of this machine—for example, the fixed rate and indifferent pressure control—it proved simple and reliable in use and gave efficient ventilation with only minor signs of CO_2 disturbance, as judged by clinical, biochemical, and fluoroscopic evidence. The cuffed tubes used were of a modified Machray pattern, for which the British Oxygen Company made me a special rubber flange fitting tightly over the tube and corresponding in shape to the "body" of an ordinary Parker or Cubley tracheotomy tube. This was secured round the neck by tapes in the ordinary way, so preventing the tube from slipping down either bronchus.

The patient who recovered was able to dispense with the tracheotomy tube after 11 days, and was finally discharged with only slight palatal weakness. The course of the illness in all three fatal cases was very similar—dramatic improvement after tracheotomy, gradual and then rapid rise of temperature over a period of three or four days to 106° or 107° F. (41.1° or 41.7° C.), followed by cyanosis, coma, and circulatory failure which was unaffected by noradrenaline drip or other anti-shock measures. I cannot agree with Drs. Harries and Lawes that general anaesthesia is best for tracheotomy in these patients. Certainly it gives the surgeon excellent operating conditions, but there must be more than an element of risk in giving thiopentone and a short-acting relaxant to such patients who, as the authors say, are often in poor condition. Certainly we have met with no major difficulty when using local anaesthesia, and I believe this to be the safest agent.

Chlorpromazine has now been shown to increase the patient's oxygen need slightly. Moreover, it can produce prolonged hypotension, and, despite its ability to give some protection against traumatic shock, different in origin from the so-called "shock" found in poliomyelitis, I think it is more likely to do harm than good. I was glad to see the authors' insistence on an adequate, trained staff. Only those who have treated such cases can appreciate fully the nursing demands. If we should be called upon to treat any considerable number of patients needing I.P.P.R. simultaneously, this would be a major problem.

To sum up, I would say that I.P.P.R. gives dramatic relief for a time, and that it is usually easy to maintain adequate ventilation and CO_2 control, but that the outcome of the illness depends upon the extent to which the virus invades the medulla, pons, and basal ganglia. In two adults in whom necropsy was carried out, these were found to be extensively involved. This process is at present beyond our control.—I am, etc.,

Romford, Essex. E. JAMES.

Complication of Epistaxis

SIR,—I was fortunate in witnessing the result of a spontaneous remission of a possible fatal complication occurring in a case of severe epistaxis.

An atheromatous lady of some 63 years with a typical blood pressure (170/75) developed a minor nose-bleed which became more severe as the day wore on. In spite of some temporary remissions the bleeding continued on the following day, when, in the early afternoon, I was called to deal with the haemorrhage. By the aid of digital pressure followed by plugging with an adrenaline-soaked swab the epistaxis was finally brought under control. After six hours, however, I was again called and found the patient had again developed a brisk epistaxis. She volunteered the information that she had suddenly experienced severe dyspnoea followed by a violent coughing attack which terminated in the expulsion of an object which she showed to me. It was a perfect blood cast of the whole of one main bronchus and its first division, which must have been some 6–8 in. (15.2–20.3 cm.) in length.—I am, etc.,

Woodford Green, Essex. J. CRAUSE.

Making the Cap Fit

SIR,—During my work in several family planning clinics the problem of the patient who fails to return has been much on my mind. Sometimes one of these women returns after an absence of several years. During this time she has discontinued using her cap and has gone back to the method of coitus interruptus, with the result that she has had one or more unplanned pregnancies. These "defaulters" are nearly always the women from the poorer social strata: the very women who need our help most. As children they have been exposed to too much lack of privacy. Such women grow up with an intense prudishness and guilt about all sexual matters.

The middle-class woman will ask freely about her sexual problems and be willing to discuss them, and will demand and expect a contraceptive method which will be completely comfortable and enable her to enjoy her sexual intercourse to the full; her poorer sister, on the other hand, will have the greatest difficulty in broaching the matter at all, and will feel that it is perhaps even wrong to ask for a contraceptive that will help enjoyment of a "guilty" pleasure. If she experiences discomfort with her cap or

dislikes the paste or has some difficulty at all with the organizing of the contraceptive technique, she feels that this is her lot in life and will not complain or ask for help easily.

At a clinic we may be somewhat divorced from the reality of our patient's living conditions. It may be as well to remember that there is probably no bathroom or even inside lavatory, and that the whole family may share one room, and perhaps the cap can only be inserted in bed in the dark, or perhaps put in hurriedly hours beforehand when there may be just a moment of privacy. Where a doctor and nurse habitually work together it should be possible for them to co-operate in being imaginative in their teaching and to find out what each individual patient's difficulties and dislikes are, and to make the method of instruction more flexible to suit the patient's needs.—I am, etc.,

London, N.W.1. ROSALIE TAYLOR.

Benzpyrene and Human Carcinogenesis

SIR,—In your admirable summary of the status of the carcinogens possibly concerned in the origin of bronchogenic carcinoma (*Journal*, November 20, 1954, p. 1213), the statement is made that "there is no doubt that benzpyrene is a dangerous carcinogen to man and animals." Although there is good evidence that certain coal tars are carcinogens to the human skin, and that such tars contain benzpyrene, a substance inducing tumours in certain animal species, there is still no proof that benzpyrene is the responsible agent in human carcinogenesis. Tar contains other carcinogens, as yet unidentified, that induce tumours in the skin of the rabbit and not the mouse.[1] The atmospheric dusts, also suggested in the origin of bronchogenic carcinoma, contain some benzpyrene in certain localities, but also contain other unidentified carcinogens active in mice.[2] Assuming benzpyrene to be active in man and using this assumption to make quantitative deduction may prove to be somewhat shortsighted, and in my view is likely to hinder a solution of the problem. There is no doubt that there are many more carcinogens yet to be identified, a procedure fraught with difficulties, but it will only be possible to make any confident prediction after this basic information has been gathered.—I am, etc.,

Chicago, U.S.A. PHILIPPE SHUBIK.

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Surgical Treatment of Carcinoma of the Lung

SIR,—Mr. T. Holmes Sellors (*Journal*, February 19, p. 445) is to be congratulated upon the five years' survival rate in his patients subjected to resection. However, it would be interesting to know what proportion these formed of the total number he saw with a view to surgical treatment. In my own experience the possibility of surgery is pathetically poor, even when first seen by the physician. Post-operative pain and discomfort are too frequently comparable with that following radiotherapy.

It is essential for the profession to see this problem in perspective. During the years 1940–53 Mr. Sellors and his colleagues, after tremendous efforts, have 140 patients surviving treatment at the end of three years. It is probable that, in England and Wales, 1,500 people had their lives similarly prolonged. Meanwhile, 132,000 had been certified as dying of this cancer. The yearly toll mounts steadily. In 1953 it was 15,100. Dr. Doll and other statisticians assure us that this figure will reach 25,000 within the next fifteen years, if present trends and habits continue. This means that more than 1,000,000 of our patients and our profession will die before the end of the century.

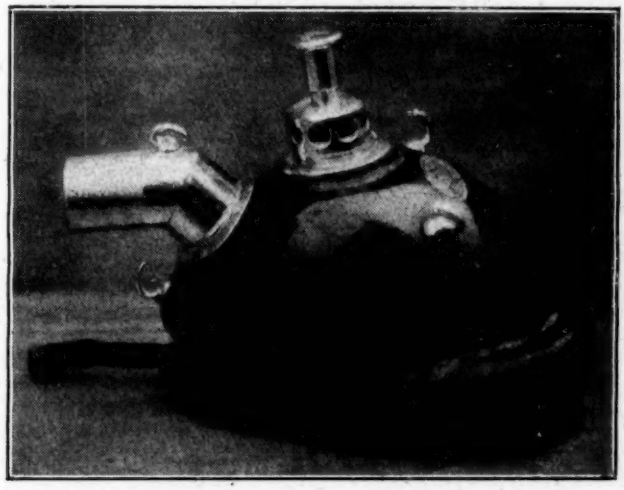
The evidence from many countries confirms the findings of Bradford Hill and Doll that tobacco consumption, especially in the form of cigarettes, is the main factor in the aetiology of this cancer. The Ministry of Health attempts to shroud this fact in mystery. The Chancellor of the Exchequer asks that the population continue to smoke, and meanwhile there is joy in the City over increased dividends from the sale of this carcinogen. Surely, Sir, it is time we asked the Minister of Health constantly to inform the population that this toll of death is preventable. No narcotic has ever caused such widespread havoc as tobacco now does throughout the Western world. The later days of the patient dying of cancer of the lung are tragic; the later years of the chronic bronchitic clutching his cigarette are pathetic. By our example and by precept we could raise preventive medicine to the place it must occupy if much lung disease is to be eradicated.—I am, etc.,

London, N.W.10. HORACE JOULES.

Salt's Valve

SIR,—I would like to write to you about the combination of Salt's valve with Langton Hewer's thyroid mask which we use at the General Hospital, Rochford.

Salt's valve is used by some anaesthetists for assisted or controlled breathing by the semi-closed method. Some find it difficult, especially when they have to keep the chin up and at the same time press upon the top of the valve with the same hand.



This can be overcome by fixing the top of Salt's valve into the hole made in the Langton Hewer's mask as shown in the figure. I would like to thank Mr. R. F. Cooper, our operating theatre technician, who made it for me and arranged for the photograph.—I am, etc.,

Rochford, Essex. P. M. MEHTA.

Chicken-pox Quarantine

SIR,—Is it really necessary to exclude children with chicken-pox from school? Every year tens of thousands of children each miss several weeks' school on account of this trivial disease, the mortality from which is virtually nil and which causes less general disturbance in a child than does the common cold. Despite the exclusion of cases from school, all but a very small number of children contract the disease before leaving. The only conceivable reason for continuing to isolate cases is the possibility of confusion with smallpox, but this is really a remote likelihood unless a case of adult smallpox has already been reported in the neighbourhood. Naturally those children who are feverish for a day or two at the onset of the disease could be kept at home until they felt better, but after this their mothers could be spared the joys of trying to keep a perfectly fit child amused all day for several weeks on end. The public would not need much educating to this new attitude; most mothers already know that the disease is a triviality and many do not bother to call the doctor if they know that there is chicken-pox about.—I am, etc.,

Margate. M. CURWEN.

Mercury and Pink Disease

SIR,—In the recent case report in your medico-legal column (*Journal*, March 5, p. 610) it is twice stated that mercury was the cause not only of the death but of the disease. Is it really true that it is now an accepted fact that pink disease is caused by ingestion of mercury?

In my late practice I had three cases of pink disease in 12 years. In two of these there was ample evidence that no mercury had ever been taken. In the third, which died, it had undoubtedly been taken. The mothers of the children who survived were members of my mothers' club and their evidence that no teething powders were given would be quite reliable. On no occasion did I or my assistant prescribe mercury in these cases. I therefore maintain that death from pink disease may be due to mercurial poisoning, but that the disease itself has another aetiology. The symptoms described in the case you quote for which the mercury was given suggest to me that the child already had pink disease.—I am, etc.,

Cockermouth. F. CHARLOTTE NAISH.

SIR,—A third inquest has been held on a child in Stoke-on-Trent who died of acrodynia associated with excessive ingestion of mercury (*Journal*, March 5, p. 610). At the second inquest in December, 1953, the manufacturers of an extensively used powder reported that mercury was being withdrawn from the formula of their products (*Journal*, December 12, 1953, p. 1330). This action has already reduced the incidence of the disease in these areas. Since January 1, 1954, however, ten cases of acrodynia (two fatal) and two cases of mercury nephrosis have been diagnosed at the major hospitals of Stoke-on-Trent and Shrewsbury. In every case there has been a history of the administration of mercury and the level of urinary mercury (estimated by Dr. E. C. Butterworth) has been high. Four patients have received grey powders on medical and one on a chemist's advice. In one case inunction of a mercury ointment was added for the skin condition. The remaining seven patients took mercury-containing teething powders.

We wish to draw attention to the fact that many of the old type of powders are still being offered for sale by retail shopkeepers. We are also concerned to find that doctors continue to prescribe a drug of dubious therapeutic value, but with known toxic properties to small infants. During 1954 the Poisons Board refused to include inorganic salts of mercury in Schedule 1 of the Poisons List. How many deaths will be required to reverse that decision?—We are, etc.,

J. G. DATHAN,
Stoke-on-Trent.
J. C. MACAULAY,
Shrewsbury.

Disk Lesions and Low Backache

SIR,—The extensive correspondence which has appeared during the past two months on the above subject has shown that there is a singular lack of unanimity in the profession in regard to the diagnosis and treatment of low back pain. One opinion it may be allowed to have established—that is, that prolapsed disk material is not the only cause of backache and the like.

I have already made some observations on the subject in a letter published in your columns (*Journal*, January 9, 1954, p. 97). I do not propose to enlarge upon them, but would like to repeat that the community has not benefited from the discovery of the association of disk lesions and sciatica as much as was hoped. Many of your correspondents have suggested that the terms lumbago and fibrositis, if not scientific, do represent recognizable clinical states. I am inclined to think it would be a good thing if we could agree to let these terms persist until we have gained a clearer view of the pathology of the conditions in question. We might then hope that the general practitioner would treat acute cases on old-fashioned lines and refrain from suspecting lesions of the disk unless there were evidence of major nerve involvement or an unusual frequency of recurrence. Such a practice would at least prevent the undesirable inculcation in the patient's mind that there was something radically wrong with his spine. It would also contribute to a reduction in the crowding of hard-worked orthopaedic clinics and ease the pressure on busy departments of radiology and physical medicine.—I am, etc.,

Faversham, Kent. MAX PAGE.

SIR,—May I be allowed to join in the controversy between those in favour of manipulation in the treatment of backache and those who are not? There are so many different clinical syndromes in backache, all of which have their typical signs and symptoms, and which often pass through different phases, but for each of them the treatment of choice may be totally different. All of these conditions may have protective muscle spasm, which may denote joint and disk changes, as one of their predominant signs. Charnley[1] has shown how a disk undergoes degeneration, and this suggests that Cyriax's[2] conception of a disk slipping in and out may be true only in a limited number of cases. Recent articles go to prove that pain in the shoulder and arm are often produced by root cuff fibrosis[3] and arthritis of the joints of Luschka.[4] Unless we see the structures involved, as we do at operation, the actual pathology must frequently be one of surmise.

However, I believe, as Cyriax does, in gentle manipulation of all painful back conditions, but with certain provisos. In certain cases rest and other forms of treatment must be instituted with the manipulation. Manipulation is not considered in an established case of true sciatica with a positive Laségue sign, absent reflexes, and impaired sensation. In a case of this type it may cause the disk to prolapse further, resulting in a cauda equina lesion. In manipulating I never allow flexion of the spine beyond a few degrees, as a flexion strain tends to force a degenerated disk backwards towards the spinal cord. Also great care is taken in hyperextension, as a piece of loose disk may be impinging on the posterior edge of two adjacent vertebrae, with the result that it may be squeezed out by this manœuvre towards the spinal cord.

That a patient may become symptom-free given a particular treatment does not necessarily signify that the right treatment has been given. For example, a young patient may recover from an attack of low back pain for which manipulation has been given, but his condition may keep on recurring. It may be that the best results would have been obtained by a period of complete rest in bed followed by periods first in a plaster cast, then in a McKee brace, and finally in a low back belt.

The non-manipulators would stress these points, but I would point out to them that often a gentle manipulation, especially if combined with physiotherapy and injections, frequently makes the patient symptom-free in one session. Besides, I believe that, unless manipulation is given, the joint movements, both voluntary and involuntary, are not restored to their normal range. For ordinary use movements require to be only 80% of normal, but when strenuous exercise is undertaken they need to be 100%. I believe that this 100% should be achieved wherever possible.

Many overlook the importance of the muscles. I believe that the muscles are affected at three different stages. In the first stage, because of postural strains, the antigravity muscles become tender. Secondly, later, as the result of postural strains, the antigravity muscles which should have been taking the strain fail in their duty, and strain is thrown on the joints which they should be supporting. As the condition of strain persists it causes changes in the joint, and a time comes when the condition produces, either gradually or acutely, a protective muscle spasm of all or of some of the muscles in an endeavour to prevent the joint being used. Thirdly, with the development of osteoarthritis the surrounding muscles undergo definite fibrotic changes.

If a positive attitude is taken by the practitioner, the patient is encouraged to help himself by home treatment, correct posture, how to avoid strain on the back, and the right attitude towards his disability. If the time factor is not important I would agree with the non-manipulators that rest, followed by a course of exercises and support, may be the treatment of choice, but I consider that gentle manipulation combined with rest, physiotherapy, injections, and support, often hasten a recovery, and I maintain support as long as is necessary. On the other hand, if one particular course of treatment, including manipulation, fails to

produce an improvement within a given time a different course is adopted according to the indications, even to immobilization in bed with traction, or plaster cast, or operation.—I am, etc.,

London, W.1. W. E. TUCKER.

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2 Ibid., 1955, **1**, 140.
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A.C.T.H. and Agranulocytosis

SIR,—Far from being unaware of the use of A.C.T.H. in agranulocytosis as your correspondents suggest (*Journal*, February 12, p. 412), we have used it in a case of *chronic* neutropenia, and this would have been apparent to Drs. D. G. Wraith and F. Dudley Hart had they read the reference (Hutchison and Alexander, 1954[1]) given in our memorandum (*Journal*, January 22, p. 207) to which their letter refers. In that case no effect on granulocyte production was evident in serial examination of both peripheral blood and marrow throughout the period of exhibition of the drug, although in other cases of a similar nature improvement has been recorded.[2 3]

In *acute* amidopyrine-induced neutropenia the theoretical indications for the use of A.C.T.H. derive chiefly from the work of Moeschlin and Wagner[4] and Moeschlin, Meyer, Israels, and Tarr.[5] These investigators provide evidence that the neutropenia is an immunological phenomenon due to elaboration by the patient of anti-leucocytic antibodies, and that the "maturation arrest" in the marrow is in fact due to exhaustion following excessive peripheral destruction of white cells instead of a direct toxic interference with the production of granular cells as had formerly been thought. A rational case for the use of A.C.T.H. could therefore be presented so long as it was believed that it depressed antibody formation in man; but now even this appears to be in doubt.[6 7] A.C.T.H. may, of course, be employed empirically or in the hope of reducing the destructiveness of antigen-antibody union in a non-specific way, but the possibility exists, in theory at least, of aggravation of the acute infection in these patients, the most serious risk to which they are exposed. In our case clinical improvement had occurred with antibiotics alone when death took place suddenly from pulmonary embolism, and it is difficult to see how A.C.T.H. could have prevented this.—We are, etc.,

H. E. HUTCHISON.
Glasgow, W.1. HUGH CONWAY.

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6 Havens, W. P., *et al.*, *J. clin. Invest.*, 1951, **30**, 647.
7 Dacie, J. V., *The Haemolytic Anaemias*, 1954. Churchill, London.

Silver Stool Sign

SIR,—It would be unfortunate if the striking condition described as silver or aluminium paint stool were to become associated with any one pathological process whether benign or malignant. In this laboratory I have seen a few watery stools which, when shaken, gave an appearance strongly reminiscent of aluminium paint, but I have seen very many more showing the same sheen or lustre but to a less striking degree. Such appearances have always been associated with the finding of fatty acid crystals in wet films examined microscopically, the number of crystals present varying with the degree of sheen as seen with the naked eye. Fresh or altered blood has not been recorded.

In a fluid stool a swirling motion serves to emphasize the less obvious degrees of this condition, and there can be little doubt that the acicular fatty acid crystals provide the physical basis for this curious appearance. A similar shimmering lustre may be seen in old exudates which contain large numbers of cholesterol crystals. The streaming effect of the fluid would seem to impart uniform shifts of alignment among the crystals, which, like a shoal of fish in a stream, now flash broadside and a moment later almost disappear as they twist along the line of sight.

This excess of fatty acid crystals in either a formed or watery stool may have many pathological causes, but in the everyday routine specimens submitted to this laboratory, which deals mainly with cases of suspected infectious disease, I have come to associate these naked-eye or microscopical appearances with the condition (or conditions) variously known as epidemic nausea,[1] the winter vomiting disease,[2] viral gastroenteritis,[3] etc. In its epidemic or sporadic form this disorder may attack very large numbers of children and adults, but few of these consult their general practitioner, and consultants may never see cases outside their own domestic circle. Many samples of faeces received from such cases do not show fatty acid crystals, and it is difficult to guess at the incidence of this change at some stage of the disease, but experience in this area strongly suggests that these acute but benign gastro-intestinal upsets account for the vast majority of silver stools.—I am, etc.,

Reading. NORMAN WOOD.

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2 Zahorsky, J., *Arch. Pediat.*, 1929, **46**, 391.
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Medical Numismatics

SIR,—I have an old token about the size of a farthing and made of copper; on the obverse is a phoenix and above and below the words "Health restored." The reverse side has "Dr. Eady, 38, Dean Street, Soho," surrounded by a laurel wreath. According to H. R. Storer,[1] it was minted about 1820, but I have not been able to obtain any other information about it.

Many of these nineteenth century "tokens" are not in fact tokens at all, but are advertisement tickets. It is possible that Dr. Eady issued his token either for advertisement purposes or as a receipt for prepayment, to be surrendered when future treatment or medicine was given. I should be grateful to learn whether any of your readers can throw further light on Dr. Eady and the use to which his token was put.—I am, etc.,

London, W.3. G. E. B. PAYNE.

REFERENCE

1 *Medicina in Nummis*, 1930. Boston, Mass.

Water Intoxication in Hypopituitarism

SIR,—The interesting paper by Mr. V. Wynn and Dr. O. Garrod (*Journal*, February 26, p. 505) stresses the abnormality of water balance in patients suffering from hypopituitarism, and in order to avoid the complication of water intoxication they suggest that a water excretion test should not be carried out unless the serum sodium exceeds 130 mEq per litre. We should like to reinforce this timely warning and briefly record a severe attack of coma associated with water retention following a Kepler test in a patient under our care at the present time.

During the recent cold spell a lady of 56, who had had a severe post-partum haemorrhage 26 years previously, but had not hitherto been diagnosed as suffering from hypopituitarism, was referred for admission to hospital through the bed bureau with the descriptive diagnosis of "query cerebral." On arrival in the ambulance she was found to be comatose and was taken straight to the ward, where the correct diagnosis of hypopituitary coma was made at a glance by the ward sister (who had seen previous cases). Since the rectal temperature, measured with a bacteriological thermometer, was only 87° F. (30.55° C.) warmth was applied, and later on she was given an intravenous injection of glucose to combat a blood sugar level of 35 mg. per 100 ml. There were no signs of water retention and the serum sodium was 120 mEq. Cortisone was not given, and she made an uneventful recovery in a few hours.

A few days later a Kepler test was carried out in order to confirm the clinical diagnosis and the patient drank 900 ml. of water. She excreted 23% only of this test dose and gained 0.91 kg. in

weight. No change in the clinical condition was noted until 24 hours later, when she vomited, became lethargic and drowsy, showed mental changes, and then lapsed into coma. The facies appeared bloated. The blood sugar fell to 37 mg. per 100 ml., but she failed to respond to intravenous injections of glucose and remained in coma despite a blood sugar level of 92 mg. per 100 ml. Cortisone was then given by intramuscular injection at a dose of 25 mg. every six hours, and after two days' treatment she recovered consciousness. Some interesting E.E.G. records were obtained during the first attack of coma and it is hoped to report the case more fully. It seems that the first attack of coma was precipitated by hypothermia,[1] the second by water retention, and both were associated with hypoglycaemia.

The response to treatment with intravenous glucose solution varied, and we suggest that in all cases of hypopituitary coma a search should be made for a precipitating cause and appropriate treatment given as well as correcting any hypoglycaemia.—We are, etc.,

S. R. F. WHITTAKER.
T. P. WHITEHEAD.
H. A. SALMON.

Warwick.

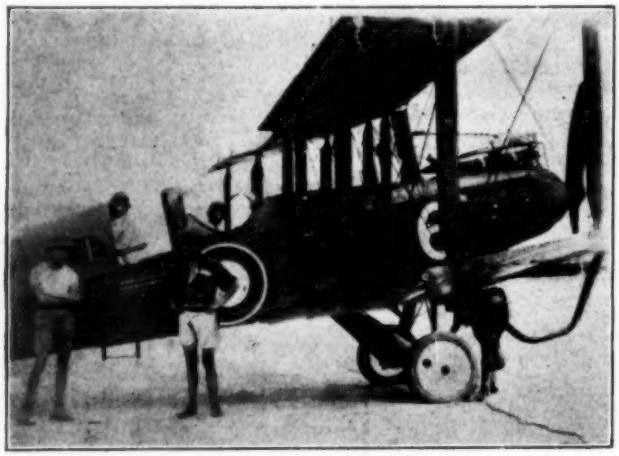
REFERENCE

1 Sheehan, H. L., and Summers, V. K., *British Medical Journal*, 1952, **1**, 1214.

First Air Ambulance

SIR,—This is an enlargement of a snapshot taken in Somaliland in January, 1920, and is a photograph of the first ambulance aeroplane ever used.

The ambulance was designed at the request of Air Vice-Marshal Sir William Tyrrell, then Wing-Commander, and principal medical officer of Z Expedition to Somaliland



("Mad Mullah" campaign). The machine, which was a D.H.9, was brought to Berbera in a large crate aboard the aircraft carrier *Ark Royal*, and was assembled on land. The fuselage was converted so that it could accommodate a stretcher and one or two orderlies. It had a hinged as well as a part sliding roof.

I had instructions from the wing-commander to have it tried out at the first opportunity, and the few trial runs we had proved that it would be quite comfortable for the patient. I did not know until afterwards that the pilot had some doubts about its airworthiness. It eventually proved a great success in taking casualties from the front line to the base in a little over two hours—a journey which by camel transport would have taken from 10 to 14 days.—I am, etc.,

London, W.1. MICHAEL SMYTH.

Experiments on Human Beings

SIR,—In your leading article (*Journal*, February 26, p. 526) you mention the "split" between the "scientist" and the "doctor," now supposed often to reside within the same personality. I take it that it is common ground that there is no more fundamental matter for both doctors and patients than assurance that the doctor will place the interests of the individual patient before the interests of "all the world." The confidence of the public in its hospitals and in doctors, within and without their walls, must surely demand no compromise with this assurance. Since the split you mention undoubtedly exists, and since advancement in the hospital service is at least closely correlated with the publication of papers, the temptation to allow the scientist to persuade, or overrule, the doctor must be increasingly substantial when the two are indeed but one. This being so, the safeguarding equitable principle that a trustee should, if possible, have no interest which conflicts with his duty (to keep paramount the welfare of the beneficiary) suggests that it is undesirable for any medical officer to experiment on his own patient: thus permission—given with the full knowledge of the nature of the experiment—would first be sought from the patient's doctor (who should not participate in the experiment). The doctor would then attempt to explain to his patient. Any experiment would be on the consenting patient of some (other) consenting doctor. Such a safeguard would allay the present public concern over the recent publicity, and would ensure that consent was valid—that is, with full explanation. Such explanation to non-medical persons alone must often be difficult or merely a mockery.

If "science" be slowed as a result of recognizing the right of the patient in this sense, then, I submit, the slowing must be cheerfully accepted. The principle is vital: any tinkering most dangerous. When the individual patient under consideration is not to benefit, but only possible future patients, the onus on the experimenter is even greater, as you point out. The recent public disclosures must surely demand at least that the profession promptly and authoritatively reaffirm the essential requirement of valid consent. The incriminated paper has not been the sole, regrettable, exception—other papers in the last three years share the opprobrium; this point was made in Parliament.

Finally, may I quote the address of Professor Pulvertaft[1]: "We have inherited a degree of trust more entire than that given to any other group of men." The author shows the consequences of forfeiture of this trust.—I am, etc.,

Sheffield. JOHN L. EDWARDS.

REFERENCE

1 *Lancet*, 1952, **2**, 839.

Isophane Insulin

SIR,—I wish to support Dr. E. B. Kraus in his defence of N.P.H. (isophane) insulin (*Journal*, February 19, p. 478). Through the courtesy of Messrs. Eli Lilly and Co., Ltd., I had the opportunity of using this preparation in 1952 and 1953, before it became available commercially. Although the number of cases (10) in which it was used was small, the trial was a severe one, because it was confined to pregnant diabetics.[1,2] In such cases, insulin requirement is usually high, so that smooth 24-hour control is difficult to attain by means of a single daily injection. Yet, with N.P.H. insulin alone, good control was maintained throughout all stages of pregnancy in seven cases. In the remaining three cases, hyperglycaemia after breakfast necessitated the addition of soluble insulin which is miscible with N.P.H. The following examples will illustrate the smoothness of control (Case No. 12 had syphilis and active phthisis).

Case No.	Maturity	Dose	Blood Sugars				
			Fasting	11 a.m.	3 p.m.	8 p.m.	11 p.m.
20	36	128 N.P.H.	145	155	170		
19	34	72 ,,	115	140	95	90	83
16	34	78 ,, and 28 sol.	120	91	83	100	91
12	32	52 N.P.H. and 24 sol.	165	150	95	125	140

In no case was there evidence of escape from control during the pre-breakfast period. Published reports[3-5]

indicate that the action of N.P.H. continues throughout the full 24-hour period.

It is apparent that the timing of N.P.H. action is far superior to that of globin and P.Z.I. There is considerable similarity between the actions of N.P.H. and "lente." In a proportion of cases N.P.H. needs the boosting effect of soluble insulin just as many cases need a mixture of semi-lente and lente. The lente group may possess an advantage in the availability of the ultralente preparation to assist in the control of cases which need intensive insulin action during the last four hours of the 24-hour period. However, with N.P.H., few cases seem to escape from control at this phase of the day. The essential difference appears to be the absence from the lente preparation of any protein or peptide material other than insulin itself.—I am, etc.,

Sunderland. M. I. DRURY.

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4 Peck, F. B., and Kirtley, W. R., *N.Y. St. J. Med.*, 1950, **50**, 2182.
5 Baganz, H. M., *et al.*, *Amer. J. med. Sci.*, 1951, **222**, 1.

Hydrocortisone Ointment in the Eczemas

SIR,—I was very interested to read Dr. Ronald Church's article (*Journal*, February 26, p. 517) on "Hydrocortisone Ointment in the Eczemas." It seems clear that hydrocortisone ointment is capable of reducing the eczema reaction in most circumstances. In some cases little or no response occurs, and it is obviously important to consider the factors that may influence the effectiveness of the application.

Considering first the preparation itself, Dr. Church is of the opinion that in circumstances where the 1% ointment was ineffective the 2.5% was also ineffective. This has not been my experience, and, in a number of patients with infantile eczema treated on one side with 1% and the other side with 2.5% preparations, improvement has been more marked on the latter side. The base of the ointment seems important so far as the physical characteristics of the application affect the condition treated, but it does not appear to influence the specific effect of the hydrocortisone. The frequency of application may also modify the effect of the ointment. An application once per day may keep a mild eczema under control, but in more severe states four times per day has been found to be more effective than twice per day.

Dr. Church mentions that eczema in certain sites of the body does not respond so readily as in others. He considers that this is related to the thickness of the epidermis affecting penetration, and obviously this must be an important factor. He mentions that there is little response in palmar eczema, and I would agree with this, although I have also noticed that neither the front nor the back of the fingers shows much improvement, suggesting that there may be some other factor in addition to the epidermal thickness. Perhaps penetration occurs more readily in warm, greasy, or moist sites. It is also possible that the hormone has a different quantitative effect on different areas of skin.

In Dr. Church's series weeping stages responded better than lichenified eczema, and again he suggests that this is due to poor penetration. He may well be right, but I think he has been rather unlucky in his results with lichenified eczema and lichen simplex, as a high percentage of such patients I have treated showed improvement. The itching was often relieved very quickly, but, as was expected, the eruption took a long time to clear, since, apart from the thickened skin, many months of an itching and scratching habit had to be counteracted. The severity of the eczema reaction influences the apparent response. The more severe attacks may "swamp" the effect of hydrocortisone. For example, in a patient who showed an improvement of the eczema on one arm treated with hydrocortisone and none on the other arm treated with the inert base, a sudden general exacerbation led to both arms becoming worse, and at this stage no difference in the severity of the rash on the two sides was apparent. Finally, there is, as one would expect, a considerable personal variation in response of the skin to the hormone. Similar patches of eczema in the same sites show for no apparent reason a difference in response from one patient to another.

I would like to thank Dr. Church for reporting his experiences with hydrocortisone. The hormone is obviously going to have an important place in the treatment of eczema in its various clinical patterns, and it is through such reports that we shall gradually discover the indications, limitations, and best methods of application.—I am, etc.,

Bristol. ROBERT P. WARIN.

Doctors and the Press

SIR,—In the *Journal* of March 12 (p. 677) is published an intimation that the chairman of the Public Relations Committee has invited representatives of the Press to attend an "exploratory meeting" on March 29 at B.M.A. House to discuss "the relations between the medical profession and the Press, particularly with reference to news from hospitals." This invitation arises from correspondence in *The Times* initiated by a letter over the name of Dr. Robert Forbes, secretary of the Medical Defence Union, wherein he accurately described the legal and ethical obligations that each doctor must observe when he is entrusted with advising and treating a patient at home or in hospital. He stressed the obligation of professional secrecy, of regarding the patients' interests as paramount, and of avoiding unethical advertisement. He also allied himself with Professor Aird in denouncing the unseemly behaviour of certain representatives of the Press when seeking to acquire information concerning the health and treatment of the conjoined Gray twins.

I also have learned of some of the devices which members of our profession were driven to adopt to protect the privacy of the treatment and the interests of the patients. This knowledge justifies me in saying that the castigation of certain representatives of the Press administered by Professor Aird in his letter to the *Observer* is well merited. It was therefore gravely disappointing for me to read a letter in *The Times* by Mr. John Pringle, the Public Relations Officer of the British Medical Association, which seemed to impute that the surgeons concerned bore some responsibility for what occurred through a failure to approach him or to accept his offer of help. He writes: "We could and would have arranged for the orderly issue to the Press of that minimum of news which rightly or wrongly . . . the Press have come to expect on these occasions having due regard all the time to the wellbeing of the patients, the feelings of the relatives and the ethical position of the doctors" (no mention is made of the legal responsibilities of the doctors). Several correspondents have protested vigorously at the unjustifiable invasion of the private lives of citizens when they are often undergoing serious mental stress from some misfortune they have encountered. Sir Linton Andrews in his letter says: "This first question is how far the Press is justified in reporting physical abnormalities that are certain to be a source of distress in the families in which they occur." The cultivation of a public interest in pathological abnormalities and their associated human distress in my view offends against the decencies of life. This is an important professional issue—a crucial issue that cannot be burked. I feel Dr. Forbes more accurately described the feelings of the rank and file of our profession when he wrote: "Every fair-minded person will surely agree that it is wholly improper for representatives of the Press to exploit the medical misfortunes of others and especially when the methods employed to collect information create impossible situations for the medical and nursing staffs of our hospitals."

May I conclude by expressing the hope that our representatives at the forthcoming conference will refuse to capitulate to the importuning of the Press or to compromise on the basic legal and ethical obligations that practitioners must discharge if they are to serve the best interests of their patients and the highest ideals of our profession? I urge our representatives strongly to present the view that the physical and mental misfortunes of our patients do not constitute legitimate "news" for dissemination to the public.—I am, etc.,

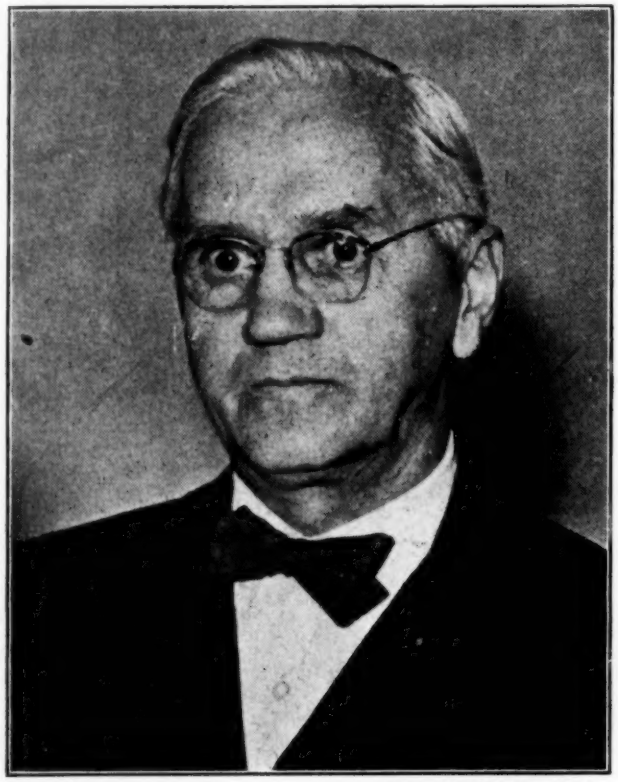
London, N.W.4 R. W. COCKSHUT.

Obituary

Sir ALEXANDER FLEMING, M.D., D.Sc.

F.R.C.P., F.R.C.S., F.R.S.

Sir Alexander Fleming, who died suddenly at his home in Chelsea on March 11, will be one of the immortals of medical history for his discovery of penicillin. An element of chance came into the discovery, but Fleming himself, who was something of a philosopher, once said, "Do not wait for fortune to smile on you; prepare yourself with knowledge," and it was a prepared mind which observed one day in 1928 that a culture plate had been contaminated by a stray mould and that around the contaminated culture was a ring of dead bacteria. It was an occurrence that would have meant nothing to many bacteriologists, but to Fleming the observation proved to be as significant as the singing kettle of James Watt or the falling apple of Isaac Newton. Fleming, essentially a humble man, was the first to acknowledge that full success was not possible without the help of others, and it was Sir Howard Florey and Dr. Ernst Chain, with their team at Oxford, who 10 years later took penicillin from the laboratory and brought it to the bedside. "The resuscitation of penicillin as a chemotherapeutic remedy," said Fleming, "is due to the brilliant work of Florey and his colleagues at Oxford."



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Behind his taciturn manner and homely speech was a spirit of great modesty. The bacteriologist is almost necessarily a modest man. At his laboratory bench he is largely the "back-room" worker in medicine. The limelight rarely shines upon him. From the discovery of penicillin onwards Fleming had to accept with what composure he could—sometimes perhaps with wry amusement—the role of great man upon whom honours, including the Nobel Laureateship in Medicine (jointly with others), came pouring from many universities and academies. "Reporters, broadcasts, speeches come hard when you are over 60," he said a few months ago when the Duke of Edinburgh made a presentation to Sir Alexander to mark the silver jubilee of the discovery of penicillin. But through it all he remained the Scot, the son of Covenanting stock, greatly embarrassed at having to accept fellowships and doctorates and freedoms and other awards and to be acclaimed as one of the great benefactors of humanity. As Louis Pasteur, whose career in some ways his own resembled, yearned for the smell of his father's tannery in the Jura, so Fleming to the end of his life never forgot the Ayrshire farm on which he was brought up. "I might have followed in my father's footsteps," he once said, "and have become a farmer, but fate decided otherwise."

Alexander Fleming was born in a humble farm home at Lochfield, near Darvel, in Ayrshire, on August 6, 1881. His father died when Alexander was only 7 years old. The boy went first to a tiny school on the moor, then to the village school at Darvel, from which he passed to Kilmarnock Academy. At the age of 14 he made his way to London, where there lived an elder brother who had already studied medicine at the University of Glasgow. In London he continued his education for two years at the Regent Street Polytechnic, and then, for economic reasons, took up work as a clerk in the office of a shipping company—not the least important part of his training, as he said afterwards.

Savings from his salary as a shipping clerk and a succession of scholarships helped him on his way as a medical student. In 1902 he entered St. Mary's Hospital Medical School. The choice of the school was fortuitous, the reason being that he was a keen swimmer and St. Mary's happened to have an active swimming-club. He won almost all the class prizes, including the senior entrance open scholarship in natural science, and he was described by a contemporary as "the most brilliant examinee ever known." He qualified in medicine in 1906, and two years later took the degrees of M.B., B.S. of the University of London, graduating with honours in physiology, pharmacology, medicine, pathology, forensic medicine and hygiene, and winning the University Gold Medal. He had a phenomenal memory, which, it was said, made him able to absorb a textbook at a single reading. It was evident that this young man from the land of Burns had a promising future. At the age of 28 he obtained his F.R.C.S. As Sir Zachary Cope has since written, "Surgery might have gained what bacteriology would have lost. Yet surgery gained infinitely more, as things fell out."

Work with Almroth Wright

The turning-point for Fleming was his meeting with one whom he called the greatest of British bacteriologists, the late Sir Almroth Wright, who died in 1947 at the age of 85. With him he worked in close association for 40 years until Wright's death. But for that meeting with Wright, he once told an audience, "it is quite likely that I would not have been a bacteriologist, and if I had not been a bacteriologist I would not have discovered penicillin." It was at St. Mary's that Wright continued his studies of therapeutic inoculation

after his epoch-making work in the Army with anti-typhoid vaccine, and he gathered round him a band of brilliant men, of whom Fleming was one. For many years Fleming continued to be, so to speak, a planet in Wright's solar system, though he also did work on his own initiative. From 1906 to 1914 onwards he was writing on the opsonic index, on vaccine therapy, and on the Wassermann reaction and salvarsan treatment.

Fleming was assistant bacteriologist at St. Mary's from 1906 to 1919, when he became assistant director of the Inoculation Department. From 1911 to 1919 he was also pathologist to the London Lock Hospitals. In 1920 he was appointed lecturer in bacteriology to the Medical School of St. Mary's, and eight years later he became professor, a chair which he occupied until 1948, when he retired as emeritus.

From 1900 to 1914 Fleming was a private in the London Scottish (T.A.) and was a member of the regimental team which won the *Daily Telegraph* Cup at Bisley in 1908. During the first world war he served in the R.A.M.C., but the association with Wright continued. They worked together at a research laboratory which was housed in the casino at Boulogne. It was here that the saline pack for the treatment of war wounds was introduced. Fleming's wartime publications included papers on the bacteriology of septic wounds, blood transfusion, and influenza; and later he contributed to the *Medical History of the War*. For his war services he was mentioned in dispatches. After the war he returned to St. Mary's. In 1919 and again in 1924 he was Hunterian Professor at the Royal College of Surgeons, and in 1928 he delivered at the Royal College the Arris and Gale lectures on lysozyme, his studies in which began in 1922, when he gave a paper on the subject to the Royal Society. If he had not subsequently discovered penicillin he would have still had a high reputation for his work on this enzyme, an antibacterial agent present in many animal fluids and especially in tears. Fleming was now acknowledged to be in the front rank of bacteriologists; it was said that he knew his bacteria—which he usually called microbes—as a shepherd knew his sheep.

For about ten years before he retired in 1946 Sir Almroth Wright was principal of the Institute of Pathology and Research at St. Mary's Hospital Medical School. Because of financial changes after the second world war this institute did not develop as originally planned and eventually lapsed. But the Inoculation Department at St. Mary's was renamed the Wright–Fleming Institute and Fleming was appointed to succeed Wright as its director. He retired from this post at the end of last year, being succeeded by Professor Robert Cruickshank, but he had no intention of giving up research work at the institute, which he visited regularly until the time of his death.

The Discovery of Penicillin

One day in September, 1928, Fleming had been examining an agar plate culture of staphylococci with the plate microscope, which entailed frequent exposure to the air. When, after a few days, he looked at the plate again he found a mould on it, and round the mould the staphylococci were dissolving. This was very unusual, so, as he himself said, "I made some investigations and the more I investigated it the more interesting it became. I found that the mould made a powerful and non-poisonous antiseptic which I christened penicillin. With the subsequent purification of penicillin I had nothing to do."

Fleming's paper on the subject, published in the *British Journal of Experimental Pathology* in 1929, was "On the Antibacterial Action of Cultures of a Penicillium with Special Reference to their Use in the Isolation of *B. influenzae*."

It was an extraordinary chance whereby the right mould contaminated a culture of the right bacteria, that it was Fleming, and not some uninterested bacteriologist, who observed it, and that Fleming that morning was not preoccupied with other things and did not throw the culture impatiently away. Thus the name penicillin was given to the antiseptic agent which the penicillium mould secreted, and the name is now as familiar as any name in medicine.

Fleming made observations on the inhibitory properties of this new substance against many species of bacteria, and he showed that the unconcentrated culture could, even when diluted some 800 times, inhibit the growth of pathogenic cocci and that it was not toxic to animals. In his summary of this paper he suggested that the new penicillin might be an efficient antiseptic for application to or injection into areas infected with penicillin-sensitive micro-organisms.

But there were many difficulties in the way. It was not at that time recognized by Fleming or anyone else that the new substance could be used to destroy bacteria selectively and harmlessly within the human body. It remained more or less a laboratory curiosity until investigation into its possible therapeutic uses began in the Oxford School of Pathology in 1938. Seven years later the work was recognized by the award of the Nobel Prize for Medicine jointly to the three men most concerned—Alexander Fleming the Scot, Howard Florey the Australian, and Ernst Chain the European refugee. In 1944 Fleming and Florey had received the honour of knighthood.

Honours and Rewards

Upon Fleming himself innumerable honours were conferred. He received the Fellowship of the Royal Society in 1943, of the Royal College of Physicians of London in 1944, and of the Royal College of Physicians of Edinburgh in 1946. The honorary degree of Doctor of Science was conferred on him by three American and six European universities; the honorary degree of Doctor of Medicine by seven European universities; the honorary degree of Doctor of Laws by two Scottish universities. He was made a Fellow of important academies in many countries—Commander of the Legion of Honour in France, a Foreign Associate of the French Academy of Medicine, a Fellow of the Royal Society of Copenhagen. He was Linacre lecturer to the University of Cambridge, Cutter lecturer to Harvard University, Mayo Foundation lecturer to the University of Minnesota, Harben lecturer to the Royal Institute of Public Health and Hygiene, among others. From the last-named institute he received the Harben Medal, the first recipient of which, in 1895, had been Louis Pasteur. He was awarded, jointly with Florey, the Gold Medal of the Royal Society of Medicine in 1947. He had previously been president of the section of pathology and of the section of comparative medicine of the Society, of which he was elected an Honorary Fellow eight months ago. In 1951 he was elected Lord Rector of the University of Edinburgh, in which office

he was succeeded by Sir Sydney Smith in 1954. A Convocation member of the Senate of the University of London from 1950, he was also a member of the Board of the Faculty of Medicine. In 1945 he was president of the Society for General Microbiology, and from 1945 to 1949 he was a member of the Medical Research Council, becoming chairman in 1946 of a committee set up to arrange clinical trials of streptomycin and other antibiotics in non-tuberculous conditions. He was made an Honorary Freeman of the City of Verona in Italy on the occasion of the International Medical Congress in 1949. He was also Honorary Freeman of the burgh of Darvel, where he was born, of Chelsea, where he lived, and of Paddington, where his work was done. In the window of St. James's Church, Sussex Gardens, he is depicted in one of five medallions representing Paddington's life and history.

Fleming had other interests apart from the laboratory bench. These included painting and literature, and he was an honorary member of the Chelsea Arts Club. Rifle shooting, golf, and swimming were his other recreations, and he did much of the work himself in the garden of his country house at Mildenhall, in Suffolk.

He married, first, Sarah Marion McElroy, of County Mayo, by whom he had one son, Dr. Robert Fleming. The first Lady Fleming died in 1949. His second wife was Dr. Amalia Coutsouris, a Greek bacteriologist who had come to work on the staff of the Wright–Fleming Institute in 1947, and had returned to Athens in 1952 to become head of the bacteriological department of a hospital there. She had won great respect for her bravery during the war in helping the British and New Zealand soldiers in the Greek campaign, and she was eventually captured and imprisoned by the Germans. Sir Alexander Fleming visited Athens in 1952, when he was presented with the freedom of the city and its gold medal, and he married Dr. Coutsouris in the following year.

Although penicillin was given to the world as a therapeutic remedy by the brilliant work of Florey and his colleagues at Oxford, Fleming's name will always be associated with its discovery, and it was the discovery of a man working alone. In an address to students near the end of his life he said, "It is for you to create the free atmosphere which will allow genius full play. . . . Much in the future of humanity depends on the freedom of the researcher to pursue his own line of thought."

We are indebted to Sir HENRY DALE, O.M., for the following appreciation: One is inclined to expect that the opinion of the world at large will be somewhat capricious in its selection of scientific discoveries for general recognition and acclaim, and even in its allotment of credit among those who at different stages, or from different angles, have contributed to the result which has made a discovery famous. Experience suggests that the original discoverer, the man "who fished the murex up," is too often almost forgotten, so that credit comes to be given, not unworthily, but too predominantly, to those who have seen and given effect to its practical potentialities. We may be glad that no such deficiency can be suggested in the recognition which public opinion has everywhere given so spontaneously to the original discovery of penicillin, in 1929, by Alexander Fleming. The world has surely made no mistake in regarding the discovery of penicillin, and its introduction into therapeutics, as providing one of the outstanding landmarks in the progress of medical science and its applications, even in an age in which that progress is acquiring, in so many directions, so astonishing a speed. For us who were Fleming's friends, still saddened by the thought of his sudden going, but thinking of the great work done so well, this is no time for argument, or for the allotment of credit between the man who first saw the penicillin phenomenon, recognized its interest, and studied it further with the instinct of a bacteriological and medical naturalist, and those others who, a whole decade later, first saw the possibility of what proved to be its immense importance in practical therapeutics—immense, surely, beyond any expectation of theirs—and whose researches carried it through the difficult stages to practical trial and launched it upon its beneficent career of healing.

We should rather rejoice, I think, that, for once in a way, all that penicillin has come to mean directly for the prevention and healing of infections, and even the new and successful quest which it inaugurated for other antibiotics, have become so largely impersonated, in the mind of the world at large, and in the figure of the quiet, devoted, rather dour, but always friendly bacteriologist, working loyally under Sir Almroth's inspiration and by his methods, contributing his own ingenious developments, and showing now and then a gleam of interest in phenomena of a different kind, discovering and investigating lysozyme, and then penicillin, with the eye and the enthusiasm of a naturalist.

The public have fully recognized the romantic features of the story. Those of us who belong to the community of medical research are apt to find more interest in what has seemed something of a puzzle—in the fact that Fleming, having discovered penicillin, having recognized its special properties as an antibacterial agent harmless to leucocytes, and having, apparently, made a tentative observation on the application of the crude medium containing it as an external antiseptic, left the discovery there and took more interest in the value of penicillin as a selective constituent of a culture medium than as, potentially, an internal antiseptic. I think that the main clue, at least, is to be found in the fact that neither the time when the discovery was made, nor, perhaps, the scientific atmosphere of the laboratory in which he worked, was propitious to such further enterprise as its development would have needed. Repeated failure had caused opinion then to harden, almost into a settled conviction, against the possibility of a successful chemotherapy of the common bacterial infections. Sir Almroth Wright himself had no belief in such a possibility. Even when some years later the introduction of sulphanilamide and its derivatives had removed the grounds for such scepticism, Wright, as Dr. Leonard Colebrook tells in his biography, was not impressed by the tremendous change which their coming had produced, even though it helped to prepare the way for Florey and Chain's new investigation, in 1939, of the possibility of preparing penicillin on a larger scale and purifying it sufficiently for practical trial, with the triumphant success that all the world knows.

But, though Fleming had thus put penicillin aside for a time, had almost forgotten it, perhaps, in the interest of the researches on other lines to which he had then returned, it is good to think that he lived not only to see the evidence of its immense practical value, on a scale so far beyond any which could have been predicted, but to receive so full a measure of the gratitude and admiration with which the world has greeted this wonderful gift of research to the health of mankind. His ashes, we learn, are to be buried in St. Paul's, but his name will surely live for evermore.

We are indebted to Professor ROBERT CRUICKSHANK, principal of the Wright–Fleming Institute of Microbiology, for the following appreciation: Pasteur has written that in the field of observation chance only favours the mind prepared and that there are no accidents in science. Fleming in his characteristically modest way often spoke about his "lucky chance" in the discovery of penicillin, but his own description of that dramatic happening rather supports Pasteur's dictum:

"A mould spore, coming from I don't know where, dropped on the plate. That didn't excite me, I had often seen such

contamination before. But what I had never seen before was staphylococci undergoing lysis around the contaminating colony. Obviously something extraordinary was happening.

"With the background that I had, this was far more interesting to me than staphylococcal research, so I switched promptly. I am now glad that for years my interest had been directed to antiseptics and that some years before I had found in a somewhat similar manner another naturally occurring antiseptic, lysozyme. But for that previous experience it is likely that I would have thrown the plate away as many bacteriologists must have done before. . . . Instead of casting out the contaminated culture with appropriate language, I made some investigations."

It was his perceptiveness added to his earlier work on antiseptics and lysozyme, with the ingenious techniques he devised for testing their activities, that allowed him to assess and prognosticate so accurately about the value and use of penicillin at the time of its discovery.

Fleming was a born biologist, keenly observant of natural phenomena and intensely curious to know how things work. His apprenticeship with Almroth Wright was a great stimulus and inspiration to him, and perhaps in those early days he was to some extent the technician working under the direction of the master. But if this early training taught him how to work and think about problems, Fleming soon showed that besides high intellectual ability and superb technical skill he also had originality of mind. Although he carried out a great deal of *ad hoc* research on current problems, his main interest was always the natural defences of the body—the phagocyte, opsonin, lysozyme—and the antibiotics were for him almost an interlude in the study of infection and immunity. He was particularly proud of lysozyme, the body's own antibiotic, and he was very pleased that recent studies were substantiating and amplifying some of his early work on natural immunity.

Phlegmatic Scot that he was in many ways, Fleming had a strong artistic sense. He was a beautifully neat draughtsman with the pen, and most of the diagrams in papers by himself and his colleagues were done by him. He took much pleasure in again preparing a demonstration of chromogenic bacteria growing as colours for the Queen Mother's visit to St. Mary's Hospital Medical School Centenary Exhibition last year, and in the week before his death he was busy preparing lantern slides in his own copperplate handwriting for his projected tour to the Middle East on behalf of the British Council. He willingly undertook many such visits abroad, and, if not a particularly good lecturer, his modest, diffident attitude about his achievements made him one of Britain's best ambassadors. Despite these outside commitments he continued to spend a great deal of time in the laboratory, seeing what was going on and giving useful advice on techniques and problems to all of us. We, his colleagues in the Wright–Fleming Institute, will miss him sorely, and we would express our deepest sympathy for Lady Fleming, who brought him companionship and happiness in these last few years.

We are indebted to Dr. JOHN FREEMAN for the following appreciation: It is hard to sum up the man Alexander Fleming at these close quarters of time and space. As a medical student he had swept all before him and had taken any prize there was to be had; but we never heard much of that, and he arrived in Almroth Wright's research laboratory as a very humble figure, the "little man" as he was affectionately called. He made friends easily, and kept them; but he always seemed a cryptic figure: not a talker, and seldom or never giving himself away. He was fond of card-playing, and at poker he probably never showed a card higher than was strictly necessary. His contribution to any laboratory discussion was usually in the form of Scotch grunts and terse interjections, or he reserved his words till others had talked themselves out; yet in retrospect he was usually seen to have dominated the argument—even in the days of Almroth Wright, who was a great dominator of conversations.

Fleming's chief characteristic was his humility, even under the enormous *réclame* of the public press in late years; yet he took an impish, almost a schoolboy delight in the honours showered on him by the universities all over the world. Nobody ever found him putting on "side"; he was the least pompous of mortals.

Penicillin naturally threw his earlier and preparatory work into the shade both in medical and in popular estimation, yet his laboratory colleagues may consider his beautiful demonstrations of the harmfulness of the common antiseptics when applied to our living tissues to deserve as much praise. He showed that even the slightest trace of an antiseptic in the blood stream did harm. "And yet," he burst out in one of his very rare moments of fervour, "there are at least seven hospitals in London, and Mary's is one of 'em, where they are regularly injecting this or that antiseptic into the blood stream in cases of septicaemia." He didn't get much praise for saying things like that.

The discovery of the powers of penicillin did not occur as a lightning flash of genius, but the way up to it had been built by long years of painstaking observation. He never tired of showing us culture plates showing the action of one colony of microbes in enhancing or retarding the growth of some neighbouring colony. Thus the entry of *Penicillium notatum* on to the stage had been systematically built up. Fleming was, so to speak, waiting for it.

He was, first and last, a man of the laboratory bench. He was very deft and accurate in his hand movements, and there is little doubt that he was the best technician in Wright's team; it used to be a pleasure to watch his controlled speed when handling glass in a blowpipe flame. He told me recently he was glad to be shedding all his responsibilities so that he could "muck about" at the bench once more and do real work again. His going will leave a sad gap in the organization of his beloved laboratories. We shall long miss the steadying influence of that great "little man," Flem.

PETER PATERSON, M.B., F.R.F.P.S.

Professor Peter Paterson, who was the St. Mungo professor of surgery in Glasgow University for eleven years between the two world wars, died at his home at Cove, by Helensburgh, on March 4. He was in his 85th year.

Peter Paterson, who came of farming stock, was born in 1870 and studied medicine at Glasgow University, where he graduated M.B., C.M. in 1891. Two years later, with a surgical career in view, he took the London Conjoint diploma, and in 1907 was elected F.R.F.P.S. After graduation and house appointments he continued his studies in Paris and Berlin, where he met Charles Mayo, with whom he became a lifelong friend. When he returned to Glasgow he became, with Hogarth Pringle, one of the late Sir William Macewen's hard-driven assistants, being appointed extra dispensary surgeon at Glasgow Royal Infirmary in 1895 and also demonstrator of operative surgery in Glasgow University. He was awarded a Weber-Parkes second medal by the Royal College of Physicians of London in 1897 for his essay on a method of producing immunity against tuberculous infection, and two years later he was awarded the Foulis memorial scholarship for eminence in pathology.

In 1906 Paterson was appointed visiting surgeon to Glasgow Royal Infirmary and in the following year lecturer in surgery at St. Mungo's College, becoming professor at the college in 1910. He vacated the chair at the college some two years before he succeeded the late Professor Robert Kennedy in 1924 in the St. Mungo chair of surgery at Glasgow University. He retired from the university professorship in 1935, when he was appointed professor emeritus. For many years he was

recognized as one of the leading surgeons and teachers of surgery in Glasgow. His wife died three years ago and he is survived by two sons.

J. A. G. B. writes: Peter Paterson did not take long to establish himself in Glasgow as a rapid and safe operator, with a flair for diagnosis. As a teacher he was vivid, dogmatic, and impressive. His main interest in research was cancer. For many years he carried out splenectomy (with oophorectomy in females) in these cases, followed by prolonged injections of various extracts of sheep's spleen. Many of the results were striking, but he firmly refused to publish them.

Socially his manner was rather taciturn, and he disliked "functions" of any sort. To his circle of friends he was an interesting and charming host, and he was at his best entertaining a small tea-party in his picturesque garden on a summer afternoon. Clad in an old shooting-jacket and armed with two boxes of mealworms, he would summon a flock of his bird friends to join the party, and while they hopped around his feet or perched on his knee he would discourse on their habits and character. Peter Paterson must be the last of the "master surgeons" of the early twentieth century.

J. DILL RUSSELL, M.B., F.R.C.S.

Mr. J. Dill Russell, who was well known and highly respected as a general-practitioner surgeon at Finchley before the first world war and as a medical officer under the Ministry of Health for many years after the war, died at Windsor Hospital on February 21. He was 81 years of age.

The youngest son of the Rev. William A. Russell, John Dill Russell was born at Strabane, Co. Tyrone, on August 23, 1873. After receiving his early education in Ireland he went to the City of London School and from there to University College and University College Hospital to study medicine. His undergraduate career was brilliant, for he gained many class medals and in his second year the Filliter exhibition in pathological anatomy and pathology. At the London M.B. examination he was awarded first-class honours, the gold medal in medicine, and honours in forensic medicine. In the same year, 1896, he acquired the London Conjoint diploma and in the following year he took the B.S. degree with honours and the F.R.C.S. by examination. After graduation he held the appointments of demonstrator of anatomy and obstetric assistant at his teaching hospital, and in 1898–9 he was senior surgical officer at the South Devon and East Cornwall Hospital, Plymouth.

Dill Russell's training and bent at first inclined him to a career in pure surgery, but with his warm humanity he was also interested in people. Finally, on leaving Plymouth, he decided to enter general practice at Finchley, where he proved a great success, building up a very large practice. His surgical skill and inclination, however, would not be denied, and in connexion with his general practice he did a good deal of operative surgery, acquiring a considerable local reputation for this work. In those days the general-practitioner surgeon was a well-known feature of the medical world, but was rather rare in areas like London, with its many large teaching hospitals staffed by skilled whole-time surgeons. Dill Russell was immensely popular and beloved because of his great skill as a doctor and his complete devotion to the welfare of his patients. He would be the first to admit that in this work he was greatly helped by his wife, who was equally devoted to the care of his patients and who loved to help on the administrative side. While in practice he became surgeon to the Metropolitan Police and to the Finchley and Hornsey Cottage Hospital and an examiner and lecturer under the London County Council.

The strain of a large practice induced Dill Russell to accept the post of divisional medical officer under the Ministry of Health in 1920, soon after his return from service in the R.A.M.C. in the first world war. This new work took him to various parts of England; later he became a senior medical officer in Whitehall, from which post he retired shortly before the outbreak of the second world war in 1939. He brought to this work the same high standards that he had held in general practice, and, where deficient, tried to raise the degree of skill and service in panel practice. Dill Russell wrote little and took no active part in medical politics. A member of the British Medical Association for over forty years, he was honorary secretary of the North London area in 1902–3 and of the Hampstead Division in 1904, and a Fellow of the Royal Society of Medicine. In the early days of the second world war he did valuable work on medical boards and in other ways. The outstanding features of his life were his scientific integrity, the thoroughness of his work, and his modesty and humanity. He was a great man, both in his attainments and in his character.

Dill Russell was singularly fortunate and happy in his home life, and he and his wife, a daughter of Dr. Frederick Wimberley, celebrated their golden wedding anniversary three years ago. It was a great tragedy, bravely borne, that two of their five sons were killed in the second world war. Two other sons, Mr. A. Scott Dill-Russell and Dr. Patrick Dill-Russell, have followed their father into medicine. To Mrs. Dill Russell, a devoted wife and mother, to the three surviving sons, and to his daughter we extend our sympathy.—W. G. S.

With the death of Dr. R. D. CAMPBELL at Inverness on February 23 the Highlands has lost one of its best-known and most revered physicians. He was 79 years of age. Ranald Douglas Campbell was born at Innellan, Argyll, on July 20, 1875, and was educated at Kelvinside Academy and at Glasgow University, where he graduated M.B., Ch.B. in 1898. After graduation he held resident posts at the Western Infirmary and the Royal Hospital for Sick Children, Glasgow, and was then resident assistant physician at the Belvidere Infectious Diseases Hospital for two years. In 1904 he left Scotland and settled in practice at Hobart, Tasmania, where he remained until the outbreak of war in 1914, when he sailed in the hospital ship *Kanowna* with the 1st Australian casualty clearing station. He served in Egypt and in the Dardanelles, where, as senior medical officer of his unit, he was the last to embark from Gallipoli at the time of the evacuation. He then came with his unit to England and later went to France, where he commanded the 3rd Australian casualty clearing station. He was awarded the D.S.O. in the 1916 Birthday Honours in recognition of his services during the Dardanelles landings, and while serving in France he received the Croix de Guerre in 1918, by which time he had attained the rank of lieutenant-colonel, and was mentioned in dispatches. After demobilization he acted for a time as deputy superintendent at the Western Infirmary, Glasgow, and then, in 1919, took over the practice of the late Dr. Wilson Black at Inverness, where he remained for the rest of his life. He became an honorary physician and ophthalmologist to the Royal Northern Infirmary, Inverness, and oculist to the Ross and Cromarty

and Nairnshire education authorities. He was chairman of the Inverness Division of the British Medical Association in 1929–30. For nearly 30 years at Inverness his general practice and hospital duties occupied most of his time. When he gave up his hospital work at the end of the second world war and his practice a year or two before the introduction of the National Health Service in 1948, he continued to maintain his connexion with the Royal Northern Infirmary by acting as the hospital's medical librarian. He is survived by a widow, a daughter of Dr. Gregory Sprott, of Hobart, and by two sons, the younger of whom is a consultant ear, nose, and throat specialist.

We are indebted to Mr. A. J. C. HAMILTON for the following appreciation: Ranald Campbell matched very closely one's conception of the ideal family physician. Of handsome appearance, always trim in his dress, a provocative and understanding twinkle in his eye, a shrewd and lively wit which on occasion could be pungent, precise and explicit in his speech, neat, clear, and unhurried in his writing, methodical in all he did—these were a few facets of his impressive personality. Where the welfare of his patients was concerned, irrespective of whether they lived in a mansion or a less pretentious dwelling, nothing was too much trouble, and only the best in treatment was good enough. In return he demanded the patient's trust and loyalty, and this he almost invariably obtained. If he did not, then he and the patient parted company. It was natural that the possessor of such a strong personality should have his detractors, but they were vastly outnumbered by his friends and admirers. Children seemed to trust him instinctively, while the elderly patients longed for his next visit. He kept himself abreast of medical advances by his reading and by the unashamed interrogation of those whose knowledge was more recent or more specialized. As a young man Campbell excelled in many forms of sport. In the Highlands his chief relaxation was fishing, and he knew well most of the beats on the Ness, the Beauly, the Conon, and the Blackwater.

Medical Notes in Parliament

Genetic Risks of Nuclear Tests

Three questions about the potential dangers to human beings from nuclear bomb tests were put to the Prime Minister on March 10. They asked him to take the initiative in proposing the establishment of a United Nations commission to study and assess these dangers; to propose an international monitoring service to detect test explosions; and to seek the limitation of the number of experiments and thus prevent injury to the human race through world-wide contamination of the atmosphere.

Sir WINSTON CHURCHILL stated that, according to paragraph 40 of the official report issued by the United States Atomic Energy Commission on February 15, the atomic and nuclear tests so far carried out had released only enough radioactive material into the atmosphere to cause an individual living in the United States to receive the same quantity of radiation that he would have received in having his chest *x*-rayed at a hospital. The experts whose advice was at the disposal of Her Majesty's Government saw, he was informed, no reason to dissent from this opinion. So far as the genetic effects of exposure to varying levels of radiation were concerned, he understood that an extensive programme of research was already in progress in both this country and the United States. In addition, he was informed that the Federation of American Scientists had proposed an immediate United Nations study of the potential genetic risks of nuclear weapons tests. It seemed, however, that they were envisaging dangers from a number of tests greatly in excess of those likely to be carried out in the foreseeable future.

Mr. PHILIP NOEL-BAKER (Derby, South, Lab.) asked the Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, whether he would arrange to publish the information available concerning the genetic effects of the increased radioactivity due to the explosion of nuclear weapons. Mr. J. R. BEVINS stated on March 8 that he should make it clear that, except for an area in the vicinity of the explosion, the increase in the radioactivity of the atmosphere resulting from the explosions of nuclear weapons which had so far taken place was negligible in comparison with the amount already present from natural causes. Investigations were continuing, but the Lord President was advised that these had not reached the stage where any firm conclusions could be drawn from them with regard to the possible genetic effects of radioactivity on human beings.

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked what research was being conducted on the problem of the increasing radioactive content of the atmosphere of London, and what evidence there was regarding the association between this increased radioactivity and bronchial disease. Mr. BEVINS replied that there was no evidence that there had been, during recent years, any significant increase in the radioactivity of the atmosphere, which remained mainly due to natural causes. Nor had there so far been any evidence that radioactivity was a contributory factor in the causation of bronchial cancer, but investigations were continuing into this possibility. Measurements of atmospheric radioactivity under different conditions were being undertaken at London and in other centres.

Changing Hospital Needs

Mr. F. TOMNEY (Hammersmith, North, Lab.) asked the Minister of Health why the board of governors of St. Mary's teaching hospital group, Paddington, had decided to convert the Children's Hospital to adult use. Mr. IAIN MACLEOD replied on March 7 that he understood the reason was that the board considered there was a surplus of staffed children's beds and not enough adult beds in the hospitals in this group.

Mr. TOMNEY said that the specialized assistance for children would now be more widely dispersed. Paddington, Kensington, and Hammersmith were densely populated areas, with large numbers of children. Would the Minister see if the decision could be reversed? Mr. MACLEOD replied that the decision had not yet been taken. The proposal was put forward because the board considered that on the whole the need for children's beds had diminished, which as a general proposition was true. He added, "We should beware of trying to freeze the pattern of hospital provision as it happened to be in 1948 when the scheme came in. There may well be good reasons for a change of use."

Seconding Nurses

Mr. R. W. SORENSEN (Leyton, Lab.), in a question about the recruitment of nurses, particularly for mental nursing, on March 7, asked what was being done to divert to other hospitals, where there was a shortage, the services of nurses and student nurses in London teaching hospitals, where there was a disproportionate number. Miss PAT HORNSBY-SMITH said that among other matters the Minister had it in mind to invite teaching hospitals to consider with him whether more might be done to second student nurses to mental hospitals as part of their training.

Tuberculosis Treatment in Switzerland

The MINISTER OF HEALTH told Mr. G. WILLIAMS on March 7 that 140 patients from England and Wales were being treated for tuberculosis in Swiss sanatoria under the Health Service. He said the scheme was reviewed annually, and was due for review in September. The main reason for its introduction was the long waiting-lists, but these had

been dramatically reduced in recent years, so much so that from time to time now it was almost difficult to take up the present allocation.

Fluoridation Tests

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister of Health what were the results established by recent work in the United States confirmed by the results of his pilot study into the fluorine content of the urine of adults in connexion with the fluoridation of water supplies; and what were the names of the authors and the dates and places of publication of these researches. Mr. IAIN MACLEOD replied on March 9 that the results showed that it was safe to add one part per million and that it was more practicable to decide the level of fluoridation in the light of dental surveys rather than by urinary examinations. References to all the relevant American work would be found in a recent publication of the American Association for the Advancement of Science, called *Fluoridation as a Public Health Measure*, which was published in Washington and could be obtained in London.

Chewing-gum.—The Food Standards Committee is considering certain aspects of the composition of chewing-gum.

Health Service Chaplains.—At the end of 1953 there were 106 whole-time chaplains employed in the Health Service; 92 were Church of England, 10 Nonconformist, and 4 Roman Catholic.

R.A.F. Standards.—In the medical standards for regular commissions in the R.A.F. (general duties) standards of visual acuity have been slightly raised and the standard of colour perception slightly reduced in the past two years.

Universities and Colleges

UNIVERSITY OF OXFORD

Dr. A. G. M. Weddell has been appointed representative of the University at the sixth International Congress of Anatomy to be held in Paris in July, 1955.

Dr. C. W. Carter has been re-appointed Reader in Biochemistry from October 1, 1955, to September 30, 1962.

The Hon. Mrs. Margaret A. Jennings, D.M., has been re-appointed Demonstrator in Pathology from October 1, 1955, to September 30, 1960.

UNIVERSITY OF CAMBRIDGE

The following degrees were conferred in Congregation on February 4:

M.D.—J. S. Pippard.
M.B.—J. F. Wood (by proxy), A. C. Johansson.

The following candidates have been approved at the examination indicated:

M.CHIR.—P. F. Boreham, G. L. Bunton, W. H. Davies, G. R. C. Peatfield, W. R. Probert, J. O. Robinson.

In Congregation on February 19 the degrees of M.B., B.Chir. were conferred, by proxy, on D. M. Surrey Dane and the degree of M.B. on W. S. Ogden, also by proxy.

Dr. R. N. Salaman, F.R.S., has been elected into an Honorary Fellowship of Trinity Hall.

UNIVERSITY OF LONDON

The following degrees were awarded by the Senate on January 26:

M.D.—P. V. Suckling.
M.S.—P. B. Counsell.

UNIVERSITY OF SHEFFIELD

Drs. J. L. A. Dowse and R. S. Sneath, Demonstrators in Anatomy, have resigned their appointments.

ROYAL COLLEGE OF SURGEONS IN IRELAND

The Fellowship of the College was conferred on J. S. R. M. Lavelle and F. X. O'Connell on February 18.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 26** (No. 8) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, th 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	13	0	7	0	1	11	1	6	0	
Dysentery	1,237	51	310	6	0	910	116	222	3	4
Encephalitis, acute	2	0	0	0		1	0	2	1	
Enteric fever: Typhoid	4	0	1	0		3	0	0	0	2
Enteric fever: Paratyphoid	3	1	4	0		5	1	1	0	
Food-poisoning	125	16		0		160	10		0	
Infective enteritis or diarrhoea under 2 years				16	6				6	28
Measles*	23,700	2694	283	630	45	2,099	33	66	23	422
Meningococcal infection	24	2	14	0		49	4	15	3	4
Ophthalmia neonatorum	32	2	5	0		36	8	7	0	
Pneumonia†	924	63	317	37		869	53	249	16	4
Poliomyelitis, acute: Paralytic	9	0	1	0	5	17	1	1	0	
Poliomyelitis, acute: Non-paralytic	1	0				7	2			
Puerperal fever§	220	49	8	1		293	49	19	1	
Scarlet fever	675	35	95	39	9	1,463	53	171	42	31
Tuberculosis: Respiratory	762	81	163	21		841	84	123	34	
Tuberculosis: Non-respiratory	107	8	23	1		125	4	22	3	
Whooping-cough	1,678	125	151	46	10	2,098	72	327	38	76

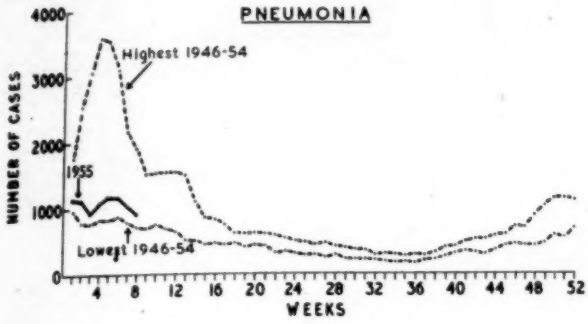
DEATHS in Great Towns	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	14	0	0	0	2	7	1	0	0	0
Influenza	81	9	5	5	5	23	4	1	0	1
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		1	0				2	2		
Pneumonia	429	68	29	34	15	375	65	24	11	7
Poliomyelitis, acute	1	0		1	0	0	0			1
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	116	15	5	2	3	101	10	26	2	9
Tuberculosis: Non-respiratory		2	0	0	2		2	1	0	2
Whooping-cough	1	0	1	0	0	1	0	0	0	0
Deaths 0–1 year	230	18	26	11	33	246	31	34	8	17
Deaths (excluding stillbirths)	7,440	1022	710	190	237	6,651	939	728	132	187
LIVE BIRTHS	7,239	1051	870	189	332	8,181	1277	949	203	311
STILLBIRTHS	180	25	24			229	34	25		

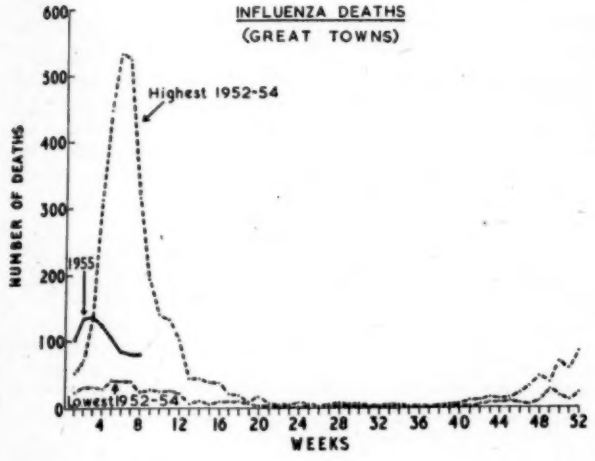
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

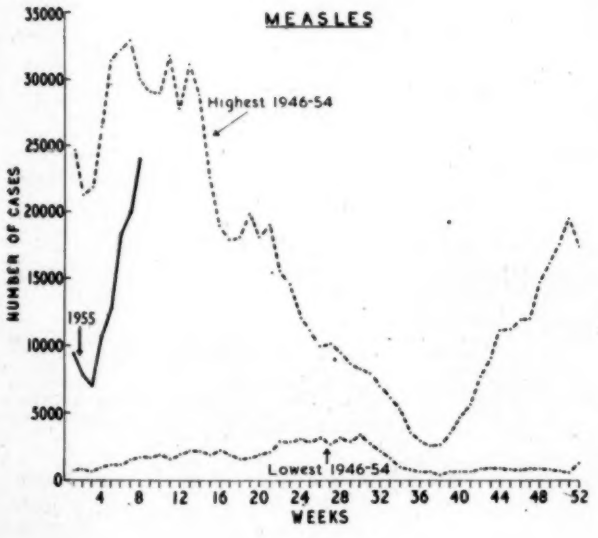
Vital Statistics

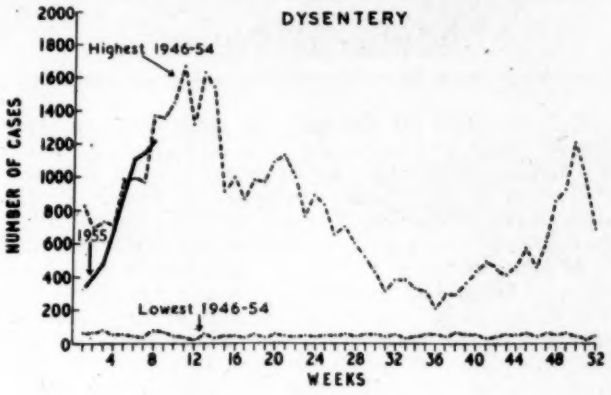
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine years 1946–54 (influenza, 1952–4) are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest variations in the trends of the notifications of infectious diseases in England and Wales during the week ending February 26 were increases of 3,724 for measles, from 19,976 to 23,700, and 92 for dysentery, from 1,145 to 1,237, and decreases of 232 for whooping-cough, from 1,910 to 1,678, and 96 for acute pneumonia, from 1,020 to 924.

The largest rises in the incidence of measles were 637 in Yorkshire West Riding, from 2,698 to 3,335; 519 in Warwickshire, from 1,060 to 1,579; 490 in Essex, from 902 to 1,392; 292 in London, from 2,402 to 2,694; 204 in Worcestershire, from 260 to 464; 189 in Nottinghamshire, from 1,086 to 1,275; 184 in Northumberland, from 590 to 774; 177 in Durham, from 843 to 1,020; 155 in Staffordshire, from 420 to 575; 143 in Surrey, from 664 to 807; 140 in Hertfordshire, from 179 to 319; 130 in Buckinghamshire, from 98 to 228; 120 in Middlesex, from 496 to 616. 675 cases of scarlet fever were notified, being 7 fewer than in the preceding week, and there were no large fluctuations in the local trends. The largest falls in the returns of whooping-cough were 41 in Staffordshire, from 92 to 51, and 34 in Kent, from 114 to 80. 13 cases of diphtheria, 3 fewer than in the preceding week, were notified.

10 cases of acute poliomyelitis were notified, and these cases were 4 fewer for paralytic and 7 fewer for non-paralytic cases than in the preceding week. The only area with a multiple case was Birmingham C.B. with 2 notifications.

The largest rises in the incidence of dysentery were 83 in Northumberland and 58 in Lancashire. The largest centres of infection during the week were Lancashire 503 (Blackpool C.B. 135, Oldham C.B. 109, Manchester C.B. 73, Blackburn C.B. 48, Lytham St. Annes M.B. 21, Liverpool C.B. 16, Darwen M.B. 16, Middleton M.B. 10, Royton U.D. 10), Northumberland 128 (Whitley Bay M.B. 28, Morpeth M.B. 27, Ashington U.D. 26, Newcastle-upon-Tyne C.B. 24), Durham 72 (Easington R.D. 15, South Shields C.B. 13, Durham R.D. 11), Yorkshire West Riding 61 (Huddersfield C.B. 20, Barnsley C.B. 11, Leeds C.B. 11), Glamorganshire 59 (Cardiff C.B. 28, Swansea C.B. 13, Llantrisant and Llantwitfardre R.D. 11), Leicestershire 57 (Leicester C.B. 27, Wigston U.D. 21), Northamptonshire 57 (Northampton C.B. 41), London 51 (Camberwell 10), Norfolk 31 (Norwich C.B. 13), Staffordshire 22 (Newcastle-under-Lyme M.B. 10), Yorkshire North Riding 21 (Middlesbrough C.B. 21), and Middlesex 20 (Edmonton M.B. 10).

Week Ending March 5

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 648, whooping-cough 1,834, diphtheria 17, measles 26,453, acute pneumonia 954, acute poliomyelitis 14, dysentery 1,265, paratyphoid fever 5, and typhoid fever 3.

Medical News

Medical Society of London.—The DUKE OF GLOUCESTER was the principal guest at the 175th anniversary dinner of the Medical Society of London held on March 8 in the Hall of the Royal College of Surgeons. Sir HORACE EVANS, the President of the Society, was in the chair. In proposing the health of the Society the Duke of Gloucester said that as an honorary F.R.C.S. he felt he was speaking on his own ground. Doctoring, he thought, must be a pretty hard life. The medical man had to keep abreast of things and be always ready for emergencies. Sir Horace Evans in reply referred to the Duke of Gloucester's close association with King Edward's Hospital Fund and many other medical institutions. He took the opportunity of thanking Dr. HOPE GOSSE and Dr. CUTHBERT DUKES for the work they had done for the Society, and also the honorary secretaries, Colonel R. DREW and Dr. E. C. SEWARD, and the registrar, Mr. PERCY MINTER.

Hunterian Link.—At a little ceremony held on March 10 at the Royal College of Surgeons Dr. W. S. C. COPEMAN, President of the Hunterian Society, presented to the council of the College John Hunter's coat of arms. The device, bearing the name of John Hunter, is fixed to the gallery of the great hall in the College's new wing; Lister's arms are at the other end of the gallery. Dr. Copeman, begging the President of the College to accept "this small tribute" from the Hunterian Society, recalled that in fact John Hunter had no arms; these were the arms of his brother William. In response Sir HARRY PLATT, P.R.C.S., said the council of the College accepted the gift with great joy. In the history of the College John Hunter had remained their great inspiration, and the presentation would form a link between the societies which reverenced John Hunter.

Royal Institute of Public Health and Hygiene.—The council announces the award of the Harben Medal, "for eminent services rendered to the public health," to LORD ADRIAN, O.M., P.R.S., and of the Smith Award, given to a medical officer of health "recognized as having done the most noteworthy work in the discharge of his official duties," to Dr. KENNETH COWAN. Both these are triennial awards. The presentations will be made at a social function at the Institute on July 20.

Fellows of University College, London.—Among the new Fellows are Professor A. BRADFORD HILL, F.R.S., professor of medical statistics at the London School of Hygiene and Tropical Medicine, Dr. A. J. MORLAND, physician at University College Hospital, and Professor SOLLY ZUCKERMAN, F.R.S., professor of anatomy at Birmingham.

Arsenic in Food.—Revised recommendations for the limits for arsenic in food have been issued by the Minister of Food in a pamphlet entitled "Food Standards Committee: Report on Arsenic" (H.M.S.O., price 4d.). Earlier reports on this subject were published in 1950 and 1951 (see *British Medical Journal*, 1950, **1**, 657). Water and milk, says the new report, should not normally contain arsenic, but a content of up to 0.1 part per million would be allowable. The following limits for other nutrients are proposed: cider, 0.2 p.p.m.; "black beer," concentrated soft drinks, ice-creams, and iced lollies, 0.5 p.p.m.; certain other foods and condiments such as dried onions, edible gelatin, chicory, and spices, limits varying from 2 to 5 p.p.m. The report states that there should be no difficulty in attaining these limits under good commercial practice, and it is recommended that statutory effect should be given to them.

Advice on Head Injuries.—A six-page clinical memorandum on the early treatment of head injuries has been prepared for the North-East Metropolitan Regional Hospital Board by its advisory committee in neurology and neurosurgery. The intention is to issue the memorandum to junior hospital medical staff in the region.

Royal College of Surgeons.—At the Council meeting on March 10 it was reported that Sir GORDON GORDON-TAYLOR had been elected a Trustee of the Hunterian Collection in place of the late Sir Arthur Keith. Sir GEOFFREY MARSHALL has been awarded the Tudor Edwards Lectureship for 1955.

Professor P. B. Medawar, F.R.S., Jodrell professor of zoology and comparative anatomy at University College, London, has been appointed to the University Grants Committee. His appointment is until December 31, 1959.

Dr. Ian MacGillivray, lecturer in obstetrics and gynaecology at Bristol, has been appointed lecturer in midwifery and gynaecology at Aberdeen.

Ladies Medical Golfing Society.—This year the society's course is Wentworth. Lady doctors and close relatives of doctors are eligible for membership. The subscription is 10s. per annum. The spring and autumn meetings will be held respectively on April 25 and September 26 at Wentworth, and there will also be matches against other clubs.

Professor L. J. Witts, Nuffield professor of clinical medicine at Oxford, will receive the honorary D.Sc. of Dublin University at Trinity College, Dublin, on July 5.

Sir Henry Cohen is to receive the honorary D.Sc. of Nottingham University at a congregation on April 22, when the DUKE OF PORTLAND is to be installed as chancellor.

COMING EVENTS

American Trudeau Society.—The 50th anniversary meeting will be held at Milwaukee, Wisconsin, from May 23 to 27. There will be papers, panel discussions, and lectures on tuberculosis and other pulmonary diseases. Details of the programme from National Tuberculosis Association, 1790, Broadway, New York, 19, U.S.A.

International Congress of Comparative Pathology.—The seventh international congress will be held at Lausanne from May 26 to 31. Among the subjects for discussion are viral diseases transmitted to man by animals, atmospheric pollution, and growth disturbances. Details from the general secretariat, 19, rue César Roux, Lausanne.

NEW ISSUES

Journal of Neurology, Neurosurgery, and Psychiatry.—The new issue (Vol. 18, No. 1) is now available. The contents include:

VARIATIONS IN THE BASOPHILIA OF NERVE CELLS ASSOCIATED WITH INCREASED CELL ACTIVITY AND FUNCTIONAL STRESS. Lárus Einarson and Erik Krogh.
ARGYROPHILE BODIES IN THE HUMAN SPINAL CORD. Marion C. Smith.
MORPHOLOGICAL NERVOUS CHANGES IN SURVIVORS OF SEVERE JAUNDICE OF THE NEWBORN. L. Crome.
UNUSUALLY SEVERE LESIONS IN THE BRAIN FOLLOWING STATUS EPILEPTICUS. A. Meyer, E. Beck, and M. Shepherd.
PREFRONTAL LEUCOTOMY AND THE ANTICIPATION OF PAIN. Alick Elithorn, Malcolm F. Piercy, and Margaret A. Crosskey.
INTELLECTUAL CHANGES FOLLOWING TEMPORAL LOBECTOMY FOR PSYCHOMOTOR EPILEPSY. Victor Meyer and Aubrey J. Yates.
VISUAL HALLUCINATIONS OF THE SELF IN ORGANIC DISEASE. Kenneth Dewhurst and John Pearson.
BASILAR IMPRESSION. D. G. Phillips.
SOME OBSERVATIONS ON THE ELECTROENCLPHALOGRAM IN CEREBRAL TUMOURS. J. H. D. Millar.
ALZHEIMER'S DISEASE WITH ACNE ROSACEA IN ONE OF IDENTICAL TWINS. Esther A. Davidson and E. Elizabeth Robertson.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 21

●BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At Wright-Fleming Theatre, St. Mary's Hospital Medical School, 5 p.m., Dr. Roger Bannister: Athletics and Physiology.
●HUNTERIAN SOCIETY.—At the Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., third dinner meeting. 8.30 p.m., discussion: An Assessment of Some New Drugs. To be opened by Sir Daniel Davies and Dr. Donald Reid. Dr. F. H. K. Green will sum up.

Tuesday, March 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: Pigmented Tumours.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture by Professor Lester Cahn (Columbia): Oral Medicine.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Oliver-Sharpey Lecture by Professor W. Melville Arnott: Order and Disorder in Pulmonary Function.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. K. I. Nissen: Pathology and Surgery of Acroparaesthesia or Carpal Tunnel Syndrome (with colour film).

Wednesday, March 23

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Symposium: Mind and Body. Speakers, Dr. J. M. Jefferson, Mr. J. T. Allanson, M.Sc., and Mr. P. T. Geach, M.A.
EUGENICS SOCIETY.—At Royal Society, 5.30 p.m., Dr. Hilda N. Lewis: Inadequate Parents and Psychological Disorders in Their Children.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Cellular Naevi and Melanomas.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann: Pathology of Otitis Media: Experimental and Human (II).
INSTITUTE OF ORTHOPAEDICS.—8 p.m., Senior Clinical Conference by Professor O. Scaglietti (Florence): Closed Treatment of Congenital Dislocation of the Hip.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. A. R. C. Higham: Diminished Fertility in the Male.
NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY.—8.30 p.m., Mr. F. A. R. Stammers: Carcinoma of the Stomach.
OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Professor C. H. G. Macafee: Clinical and Pathological Aspects of Solid Ovarian Tumours.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Joseph Clover Lecture by Professor W. W. Mushin: Measurement in Anaesthesia.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. J. H. Sheldon: Social Aspects of Old Age. (Illustrated).
ST. MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE.—5.30 p.m., Dr. E. A. Bennet: Selection of Patients for Psychotherapy.

Thursday, March 24

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Epidemiology of Fungous Diseases.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Dr. G. R. Wadsworth: Effects of Haemorrhage in Man; Dr. S. E. Keidan: C-Reactive Protein.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.15 p.m., social and annual general meeting.
LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Dorchester Hotel, W., 6.45 p.m. to 1.30 a.m., annual dinner dance.
ROYAL EYE HOSPITAL.—5.30 p.m., Dr. T. H. Whittington: Some Aspects of Refraction Work: (5) Factors Affecting Binocular Vision.
SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At Cane Hill Hospital, Coulsdon, 8 p.m., Dr. Alexander Walk: Royal Commissions Past and Present.

Friday, March 25

ASSOCIATION OF CLINICAL BIOCHEMISTS (SOUTHERN REGION).—At North Middlesex Hospital, Silver Street, Edmonton, N., 3 p.m., scientific papers.
CAMBRIDGE MEDICAL SOCIETY.—At Addenbrooke's Hospital, 3 p.m., Professor R. V. Christie: Bronchitis.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Dowling.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. Smart and Dr. K. F. W. Hinson: Pneumoconiosis.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., Mr. K. G. Rotter: Aural Vertigo.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At 11, Chandos Street, Cavendish Square, W., 7.30 p.m., short papers by Dr. A. Siboulet, Dr. Duncan Catterall, Dr. G. Mayne, Dr. R. Lees, and Dr. G. Horne.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor R. Bradlaw: De Cute Oris.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Professor E. J. Wayne: Clinical Surveys and Clinical Trials.

Saturday, March 26

INSTITUTE OF ORTHOPAEDICS.—10 a.m., clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Gray.—On March 10, 1955, at St. David's Hospital, Cardiff, to Marion (formerly Muir), wife of Dr. Peter Gray, a daughter.
Laidlaw.—On March 11, 1955, at Ronkswood Hospital, Worcester, to Greta (formerly Mair), wife of Dr. Allan J. Laidlaw, a brother for Fiona—Alistair Malcolm Lawrie.
Nathanson.—On March 9, 1955, to Margaret (formerly Milman), wife of Dr. N. E. Nathanson, a daughter.
Summers.—On March 8, 1955, at Brixworth, Northants, to Mary, wife of Dr. H. A. Hamilton Summers, a son.

MARRIAGES

Alexander—Munro.—On March 12, 1955, at Egremont, Cumberland, Conel Patrick Alexander, M.B., B.S., M.R.C.P., of the Royal Free Hospital, London, W.C., to Susan Lilias Munro, M.B., B.S., of Egremont.
Baskin—Gibbins.—On March 3, 1955, in London, Dr. Michael Baskin, of Seapoint, Capetown, South Africa, to Miss Thelma R. K. Gibbins, of Surbiton, Surrey.
Stone—Dana.—On March 12, 1955, at Christ Church, Sutton, Surrey, Arthur Richard Stone, M.B., Ch.B., M.R.C.P., of Wellington, New Zealand, to Barbara Mary Dana, M.B., B.S., of Sutton, Surrey.

DEATHS

Clark.—On February 24, 1955, at her home, 4, Overleigh, Street, Somerset, Hilda Clark, M.B., B.S., aged 74.
Cowey.—On February 17, 1955, at Barnwood House, Gloucester, Reginald Vionnée Cowey, D.S.O., L.S.A., Lieutenant-Colonel, R.A.M.C., retired, aged 81.
Densham.—On February 23, 1955, at his home, 29, The Plantation, Worthing, Alec Densham, M.B., aged 79.
Du Boulay.—On March 1, 1955, at "Chesil," Chandler's Ford, Eastleigh, Hants, Hubert Houssemayne Du Boulay, M.R.C.S., L.R.C.P., aged 94.
Garfit.—On February 23, 1955, Charles Corringham Garfit, M.B., Ch.B., of Kirby Muxloe, Leics, aged 84.
Goddard.—On February 22, 1955, at Washington, U.S.A., Calvin Hooker Goddard, M.D., aged 63.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Diagnostic Curettage in Suspected Uterine Cancer

Q.—*What is the danger of a diagnostic curettage spreading cancer cells in a patient with suspected cancer of the uterus?*

A.—Diagnostic curettage, by exposing vascular channels to malignant cells, must on theoretical grounds be accepted as involving some risk of disseminating carcinoma of the body of the uterus, although no more than the performance of biopsy on a suspicious lesion anywhere else in the body. There is nothing to show how great is the risk, but practical experience suggests it is small, since distant metastases are rare even when carcinoma recurs after curettage and hysterectomy. Vaginal metastases are now regarded as being the result of spread via the blood or lymph stream rather than by cellular spill through the cervix, and again there is no evidence to show that they are more frequent in cases subjected to diagnostic curettage before hysterectomy.

The alternative to diagnostic curettage would be to carry out total hysterectomy on every woman with symptoms at all suggestive of carcinoma, and most authorities would regard the risk of an unnecessary hysterectomy as being greater than that of disseminating a possible growth by curettage. Cytological studies carried out on smears of upper vaginal debris are not by themselves a sufficiently reliable method of diagnosis, so, for the present, curettage remains a proper procedure to exclude or diagnose carcinoma of the body of the uterus. Nevertheless, if the clinical features are such as to make the diagnosis practically certain, many gynaecologists would proceed to total hysterectomy without preliminary curettage. Others believe that if the curettings show naked-eye evidence of malignancy then there is less risk of growth becoming disseminated if hysterectomy is carried out at once rather than deferred for a few days pending microscopic examination and report.

Sequelae of Herpes Zoster

Q.—*A man of 81 who had shingles 34 years ago has now had a second attack characterized by severe pain and rash in the right arm and hand. Numbness in the area supplied by the radial nerve still persists. Vitamin B tablets are being taken without effect. What other treatment can be advised? Should not the patient have acquired immunity from his first attack?*

A.—An attack of herpes zoster usually confers lifelong immunity, but there are occasional exceptions to this rule. It is not stated for how long the patient has had his present symptoms. Apparently he is now complaining only of numbness in the area affected by the eruption, a symptom which requires no active treatment. Perhaps, however, the patient has pains and dysaesthesiae in the affected part—that is, post-herpetic neuralgia. This condition is exceedingly difficult to treat. The simple analgesics are often valueless and opium derivatives are contraindicated. Irradiation of the affected sensory ganglia with deep *x* rays is sometimes helpful and is best carried out within two or three months of the acute illness.

The results of various surgical procedures are disappointing. In a patient of this age simple analgesics and an optimistic expectancy, possibly supplemented by deep *x*-ray therapy, afford the best approach. The majority of elderly

patients recover with little or no residual discomfort. One assumes that the zoster is not symptomatic—that is, there is no pre-existent structural nervous disease.

The Evening Rise of Temperature

Q.—*Why, in most pyrexial illnesses, does the temperature rise take place in the evening?*

A.—Normal body temperature measured either in the mouth or in the rectum shows a diurnal rhythm with the lowest temperature recorded in the early morning, rising steadily to reach a maximum usually about 4 p.m., and thereafter declining again. The normal difference between the morning and evening temperature is of the order of 1.2–1.5° F. (0.7–0.85° C.). In pyrexia this diurnal rhythm is in most cases still present although considerably accentuated, so the highest temperature recorded is in the late afternoon and the evening.

There are many other diurnal rhythms apart from body temperature: for instance, the rate of urine secretion rises during the day and falls in the night, and there is a diurnal rhythm in the excretion of corticosteroids. The diurnal rhythms are found in animals and plants. All these rhythms are associated with the local environment. In the case of man the day–night rhythm is imposed from early childhood, but the rhythms can be extremely persistent, even when the pattern of activity is completely altered, so a change from a day to a night shift means that the peak of temperature is reached during sleep and the nadir after several hours of work. It may take many days, or even weeks in some individuals, for any particular rhythm to change to the new pattern. The final cause of diurnal rhythms can be reasonably concluded to be the pattern of activity of the individual, but the intermediate factors are unknown. The physiology of these rhythms provides a long and fascinating chapter of ignorance. Staying in bed does not suppress the diurnal temperature rhythm, and this has been shown by many observers. It is not surprising, therefore, that pyrexial temperatures follow the normal diurnal rhythms, although set at a much higher level.

Histamine Treatment of Migraine

Q.—*Can you please give me some information about the treatment of migraine with histamine?*

A.—Although there have been reports from the United States which suggest that the treatment of migraine with histamine is sometimes helpful, one's personal experience has been that it is of no value.

Treatment of Mongolism

Q.—*The third child of one of my patients is a mongol with all the stigmata of mongolism. He is a boy aged 9 years. What is the latest treatment of mongolism? Is glutamic acid helpful?*

A.—No satisfactory specific treatment for mongolism has yet been discovered. There is no evidence that glutamic acid has any specific role in this disorder. A satisfactory diet with adequate protein includes all the amino-acids necessary. The prognosis depends on the degree of the mongolism. Occasionally a case is described in which all the physical signs are present but the individual is of normal intelligence. On the other hand, these children are sometimes low-grade idiots. Most of them are imbecile and can learn to be useful but not economically independent. They usually do better if it is possible to keep them at home rather than putting them in a special institution. This will depend on the position in regard to the other members of the family. Attempts at education should be adjusted to the apparent mental level, though a few cases of mongolism have been able to learn to read and write and profit by more formal instruction.

Bladder Training

Q.—*At what age should a child be expected to be dry in bed? A professional couple are worried because their boy of 3½ years wets his bed every night and shows no signs of becoming dry. The parents remove the wet napkin when they go to bed, pot the boy, and he then remains dry until the morning. What preventive measures, if any, should be instituted? So far, I have just done my best to reassure the parents that there is nothing to worry about, and that treatment would be a mistake.*

A.—Most children have acquired bladder control by the age of 3½ years, but failure to do so does not imply that nocturnal enuresis will be permanent. Not infrequently there is a history in the family of delay in acquiring control, and the history may give an indication of when improvement in the boy may be expected. Routine examination of the urine is desirable to eliminate the unlikely presence of a renal condition. Other investigations are not indicated. Over-zealous "training" should be discouraged. A trial should be given to advancing the hour at which the boy is potted, and to encouraging confidence by not replacing the napkin.

Failure to Ejaculate

Q.—*My patient is a married man aged 36, strong and vigorous. He has been married about four months. His wife is aged 26. He complains that he cannot get an orgasm. There is no difficulty in the marital act. His wife seems to be completely satisfied by the act. They have intercourse four or five times a week. He is in good physical health. By occupation he is a farmer, and has no mental inhibitions or complicated ideas. In short, he is a normal, healthy, hardworking outdoor man. Please suggest a line of treatment.*

A.—These cases of failure to ejaculate are far commoner than was formerly believed. They are not due to any physical defect, for such patients are able to ejaculate in their sleep, and often have one of these spontaneous emissions in sleep on the same night as they have sexual intercourse or on the following night. As a rule the patient is unable to produce semen by masturbation, and for this reason artificial insemination with the husband's semen cannot be used as a means of satisfying the wife's desire for a child.

Despite the questioner's assurance that this particular patient has "no mental inhibitions," it is in this region of the mind that the explanation of his condition lies. Unfortunately these cases of failure to ejaculate usually prove more resistant to psychotherapy than do cases of failure to obtain an erection, but psychotherapy is the right line of treatment. It might be worth while making a trial of giving him some octyl nitrite to inhale at the time of intercourse. This has helped a few patients, but too much should not be expected of it.

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